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NEWS 18	JUL 28	EPFULL enhanced with additional legal status information from the epoline Register
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NEWS 20	JUL 28	STN Viewer performance improved
NEWS 21	AUG 01	INPADOCDB and INPAFAMDB coverage enhanced
NEWS 22	AUG 13	CA/CAplus enhanced with printed Chemical Abstracts

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                  page images from 1967-1998
 NEWS 23   AUG 15  CAOLD to be discontinued on December 31, 2008
 NEWS 24   AUG 15  CAplus currency for Korean patents enhanced
 NEWS 25   AUG 25  CA/CAplus, CASREACT, and IFI and USPAT databases
                   enhanced for more flexible patent number searching
 NEWS 26   AUG 27  CAS definition of basic patents expanded to ensure
                   comprehensive access to substance and sequence
                   information

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FILE 'HOME' ENTERED AT 15:24:37 ON 02 SEP 2008

=> FIL BIOSIS CAPLUS EMBASE
COST IN U.S. DOLLARS                                  SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                       0.63       0.63

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=> s mRNA (3a) instabil? sequence
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=> s mRNA (3a) instabil?
L2          964 MRNA (3A) INSTABIL?
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L3            0 L1 AND APP

=> s l2 and APP
L4            3 L2 AND APP

=> dup rem l4
PROCESSING COMPLETED FOR L4
L5             3 DUP REM L4 (0 DUPLICATES REMOVED)

=> d bib abs 1-
YOU HAVE REQUESTED DATA FROM 3 ANSWERS - CONTINUE? Y/(N):y

L5   ANSWER 1 OF 3  CAPLUS  COPYRIGHT 2008 ACS on STN
AN   2004:999715  CAPLUS
DN   141:406751
TI   Assay and expression systems comprising reporter gene and
instability
     sequence DNA for identifying compounds which affect stability of
mRNA
IN   Kastelic, Tania; Cheneval, Dominique
PA   Novation Pharmaceuticals Inc., Can.
SO   U.S. Pat. Appl. Publ., 49 pp., Cont.-in-part of U.S. Ser. No.
869,159.
     CODEN: USXXCO
DT   Patent
LA   English
FAN.CNT 2
     PATENT NO.           KIND   DATE        APPLICATION NO.
DATE
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PI   US 20040231007        A1    20041118    US 2004-814634
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     WO 2000039314         A1    20000706    WO 1999-CA1235
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ID, IL,
              IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU,
LV, MA,
              MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE,
SG, SI,
              SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA,
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BJ, CF,
              CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
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AU 2005229165 A1 20051013 AU 2005-229165
20050401
CA 2603585 A1 20051013 CA 2005-2603585
20050401
WO 2005095615 A1 20051013 WO 2005-CA491
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W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ,
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MR, NE, SN, TD, TG
EP 1774000 A1 20070418 EP 2005-730094
20050401
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HU, IE,
IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR
JP 2007530058 T 20071101 JP 2007-505349
20050401
US 20070190532 A1 20070816 US 2007-594851
20070504
PRAI GB 1998-28709 A 19981224
WO 1999-CA1235 W 19991223
US 2001-869159 A2 20010815
US 2004-814634 A 20040401
WO 2005-CA491 W 20050401

AB The present invention relates to an assay for the identification of biol.
active compds., in particular to a reporter gene assay for the
identification of compds., which have an effect on mRNA stability. More
particularly, the present invention relates to a reporter gene expression
system and cell lines comprising said expression system. The invention
further relates to compds. which destabilize mRNA. Radicicol and
radicicol analog A showed a clear effect on mRNA stability.
Human

APP, Bcl-2α, c-myc, TNFα, IL-1β, VEGF instability sequence were constructed. Instability sequence DNA is from The gene encoding a cytokine, a gene encoding a chemokine, a gene encoding a nuclear transcription factor, a gene encoding an oxygenase, a proto-oncogene, an immediate early gene, a cell cycle controlling gene, and a gene involved in apoptosis.

L5 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2000:5273 CAPLUS
DN 132:147542
TI Growth factor-mediated stabilization of amyloid precursor protein mRNA is mediated by a conserved 29-nucleotide sequence in the 3'-untranslated region
AU Rajagopalan, Lakshman E.; Malter, James S.
CS Department of Pathology and Laboratory Medicine, University of Wisconsin Medical School, Madison, WI, 53792, USA
SO Journal of Neurochemistry (2000), 74(1), 52-59
CODEN: JONRA9; ISSN: 0022-3042
PB Lippincott Williams & Wilkins
DT Journal
LA English
AB Using a cell-free translation system, we previously demonstrated that the turnover and translation of amyloid precursor protein (APP) mRNA was regulated by a 29-nucleotide instability element, located 200 nucleotides downstream from the stop codon. Here we have examined the regulatory role of this element in primary human capillary endothelial cells under different nutritional conditions. Optimal proliferation required a growth medium (endothelial cell growth medium) supplemented with epidermal, basic fibroblast, insulin-like, and vascular endothelial growth factors. In vitro transcribed mRNAs with the 5'-untranslated region (UTR) and coding region of β-globin and the entire 3'-UTR of APP 751 were transfected into cells cultured in endothelial cell growth medium. Wild-type globin-APP mRNA containing an intact APP 3'-UTR and mutant globin-APP mRNA containing a mutated 29-nucleotide element decayed with identical half-lives (t1/2 = 60 min). Removal of all supplemental growth factors from the culture medium

significantly accelerated the decay of transfected wild-type mRNA (t1/2 =
10 min), but caused only a moderate decrease in the half-life of transfected mutant mRNA (t1/2 = 40 min). We therefore conclude that the
29-nucleotide 3'-UTR element is an mRNA destabilizer whose function can be
inhibited by inclusion of the aforementioned mixture of growth factors in
the culture medium.
RE.CNT 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2008 ACS on STN
AN 1996:187915 CAPLUS
DN 124:252087
OREF 124:46496h,46497a
TI Interactions of INS (CRS) elements and the splicing machinery regulate the
production of Rev-responsive mRNAs
AU Mikaelian, Ivan; Krieg, Marion; Gait, Michael J.; Karn, Jonathan
CS MRC Lab. Mol. Biol., Cambridge, CB2 2QH, UK
SO Journal of Molecular Biology (1996), 257(2), 246-64
CODEN: JMOBAK; ISSN: 0022-2836
PB Academic
DT Journal
LA English
AB The human immunodeficiency virus type 1 (HIV-1) Rev protein stimulates the
export to the cytoplasm of unspliced HIV-1 mRNAs carrying the Rev response
element (RRE). However, simple addition of the RRE to β-globin pre-mRNA
does not confer a Rev response on this heterologous transcript. In this
paper, the authors demonstrate that a strong Rev response is conferred on
β-globin pre-mRNA when an inhibitory (INS) elements is inserted into
the gene together with the RRE. In the presence of the INS element, Rev
was able to stimulate the export to the cytoplasm of unspliced mRNA 10 to
15-fold. INS elements from the HIV-1 p17 gag and pol genes were equally
active in complementing Rev-dependent nuclear export of unspliced mRNA.
By contrast, mutated p17 gag INS element, known to be inactive in gag
mRNA instability assays, was unable to complement the
Rev/RRE system and stimulate nuclear export. Similarly, AUUUA-instability

elements from the granulocyte-macrophage colony stimulating factor mRNA (GM-CSF) destabilized β-globin mRNA but could not substitute for the HIV INS elements. Complementation between the Rev/RRE system and the INS elements was only observed when splicing was efficient. When splicing of the β-globin gene receptor is impaired by mutations in the 5' splicing of the β-globin gene receptor is impaired by mutations in the 5' splice donor, the 3' splice acceptor sequence, or the polypyrimidine tract, the majority of the unspliced mRNA is exported from the nucleus in the absence of Rev. In the presence of splice site mutations, Rev is able to act independently of a functional INS element and increase the export of unspliced mRNA three to fivefold. The authors propose that nuclear factor(s) binding to INS elements sep. unspliced β-globin pre-mRNA from the splicing apparatus Pre-mRNA in this "INS compartment" remains accessible to Rev. Thus, there is a synergy between the INS elements and accessible to Rev. Thus, there is a synergy between the INS elements and Rev which leads to enhanced nuclear export of unspliced mRNA.

=> FIL STNGUIDE

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	40.74	41.37

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-2.40	-2.40

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LAST RELOADED: Aug 29, 2008 (20080829/UP).

=> FIL BIOSIS CAPLUS EMBASE

COST IN U.S. DOLLARS	SINCE FILE	TOTAL

	ENTRY	SESSION
FULL ESTIMATED COST	0.30	41.67

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	

-2.40

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=> s l2 and bcl-2
L6 10 L2 AND BCL-2

=> dup rem l6
PROCESSING COMPLETED FOR L6
L7 6 DUP REM L6 (4 DUPLICATES REMOVED)

=> d bib abs 1-
YOU HAVE REQUESTED DATA FROM 6 ANSWERS - CONTINUE? Y/(N):y

L7 ANSWER 1 OF 6 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
DUPLICATE 1
AN 2008:342473 BIOSIS
DN PREV200800342472
TI The nucleolin targeting aptamer AS1411 destabilizes bcl-2 messenger RNA in human breast cancer cells.
AU Soundararajan, Sridharan; Chen, Weiwei; Spicer, Eleanor K.; Courtenay-Luck, Nigel; Fernandes, Daniel J. [Reprint Author]
CS Med Univ S Carolina, Dept Biochem and Mol Biol, 176 Ashley Ave, Charleston, SC 29425 USA
fernand@musc.edu
SO Cancer Research, (APR 1 2008) Vol. 68, No. 7, pp. 2358-2365.
CODEN: CNREA8. ISSN: 0008-5472.
DT Article
LA English
ED Entered STN: 11 Jun 2008
Last Updated on STN: 11 Jun 2008
AB sought to determine whether nucleolin, a bcl-2 mRNA-binding protein, has a role in the regulation of bcl-2 mRNA stability in MCF-7 and MDA-MB-231 breast cancer cells. Furthermore, we examined the efficacy of the aptamer AS1411 in targeting

nucleolin and inducing bcl-2 mRNA
instability and cytotoxicity in these cells. AS1411 at 5 mu mol/L
inhibited the growth of MCF-7 and MDA-MB-231 cells, whereas 20 mu mol/L
AS1411 had no effect on the growth rate or viability of normal MCF-10A
mammary epithelial cells. This selectivity of AS1411 was related to a
greater uptake of AS1411 into the cytoplasm of MCF-7 cells compared with
MCF-10A cells and to a 4-fold higher level of cytoplasmic nucleolin in
MCF-7 cells. Stable siRNA knockdown of nucleolin in MCF-7 cells reduced
nucleolin and bcl-2 protein levels and decreased the
half-life of bcl-2 mRNA from 11 to 5 hours.
Similarly, AS1411 (10 mu mol/L) decreased the half-life of bcl-2 mRNA in MCF-7 and MDA-MB-231 cells to 1.0 and 1.2 hours,
respectively. In contrast, AS1411 had no effect on the stability of
bcl-2 mRNA in normal MCF-10A cells. AS1411 also
inhibited the binding of nucleolin to the instability element AU-rich
element 1 of bcl-2 mRNA in a cell-free system and in
MCF-7 cells. Together, the results suggest that AS1411 acts as a
molecular decoy by competing with bcl-2 mRNA for
binding to cytoplasmic nucleolin in these breast cancer cell tines. This
interferes with the stabilization of bcl-2 mRNA by
nucleolin and may be one mechanism by which AS1411 induces tumor cell
death.

L7 ANSWER 2 OF 6 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
AN 2006:182353 BIOSIS
DN PREV200600184465
TI Mode of action of rituximab in chronic lymphocytic leukaemia; Activation
of Tis11b, an inducer of mRNA instability, and
induction of apoptosis.
AU Baou, Maria [Reprint Author]; Murphy, John; Jewell, Andrew P.
CS Kingston Univ, Sch Life Sci, Surrey, UK
SO Blood, (NOV 16 2005) Vol. 106, No. 11, Part 1, pp. 593A.
Meeting Info.: 47th Annual Meeting of the American-Society-of-Hematology.
Atlanta, GA, USA. December 10 -13, 2005. Amer Soc Hematol.
CODEN: BLOOAW. ISSN: 0006-4971.
DT Conference; (Meeting)
LA English
ED Entered STN: 15 Mar 2006

Last Updated on STN: 5 Jun 2008

AB Rituximab is a chimeric anti-CD20 monoclonal antibody that has been used successfully in the treatment of Non Hodgkin's Lymphoma or patients with Chronic Lymphocytic Leukaemia (CLL). The mechanisms of action of Rituximab are not fully understood although antibody dependent cell mediated cytotoxicity and complement dependent cytoxicity have been shown to be important. An alternative mechanism is the induction of apoptosis through activation of pathways mediated through CD20. CD20 is involved in many cellular processes including proliferation, activation, differentiation and apoptosis. We have found that treatment of CILL cells with 20 mu g/ml Rituximab cross-linked will) a secondary antibody reduced cell viability from 84 +/- 8% (in unstimulated cells) to 51.50 +/- 10% after 48h of cultivation by the Annexin/PI method. Using inhibitors specific for p38, JNK and ERK pathways, we found that inhibition of p38 inhibits the induction of apoptosis by crosslinked Rituximab. Rituximab has been reported to inhibit this pathway andlead to down regulation of bcl-2 expression in AIDS related lymphoma cells. However the mechanism is unclear. One mechanism by which many genes involved in apoptosis are regulated is through induction of mRNA instability through induction of Tis 11 family genes. The Tis I I family (Tis 11, Tis 11b/Berg36 and Tis 11d) bind to AU Rich elements present in several mRNA (eg bcl-2, TNF) and cause their degradation. We found that Tis 11b/Berg36 is strongly induced by crosslinked Rituximab. Tis I Id was weakly induced while Tis I I remained unchanged after treatment. Furthermore we found that induction of Tis 11b/Berg36 by Rituximab is partly regulated through the p38 pathway since inhibition of this pathway resulted partial or complete inhibition of Tis 11b/Berg36 induction. This suggests that Tis 11b/Berg36 may mediate the induction of apoptosis by Rituximab through the degradation of proteins

involved in apoptosis that contain AU Rich elements, disrupting autocrine
cytokine feedback mechanisms and down regulating bcl-2
.

L7 ANSWER 3 OF 6 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
DUPLICATE 2
AN 2005:126151 BIOSIS
DN PREV200500121589
TI Retinoid-induced apoptosis in HL-60 cells is associated with nucleolin
down-regulation and destabilization of bcl-2 mRNA.
AU Otake, Yoko; Sengupta, Tapas K.; Bandyopadhyay, Sumita; Spicer, Eleanor
K.; Fernandes, Daniel J. [Reprint Author]
CS Dept Biochem and Mol Biol, Med Univ S Carolina, 173 Ashley Ave,POB 250509,
Charleston, SC, 29425, USA
fernand@musc.edu
SO Molecular Pharmacology, (January 2005) Vol. 67, No. 1, pp. 319-326. print.
ISSN: 0026-895X (ISSN print).
DT Article
LA English
ED Entered STN: 1 Apr 2005
Last Updated on STN: 1 Apr 2005
AB All-trans retinoic acid (ATRA) induces differentiation of promyelocytic
leukemia cells, but the mechanisms by which cellular differentiation leads
to apoptosis are not well understood. Studies were done to address the
question whether ATRA-induced apoptosis is a consequence of
destabilization of bcl-2 mRNA and decreased cellular
levels of the anti-apoptotic protein, bcl-2. ATRA
induced differentiation of HL-60 cells along the granulocytic pathway
within 48 h. The half-lives of bcl-2 mRNA in HL-60
cells incubated with ATRA for 48 or 72 h were reduced to 39 and 7% of the
corresponding untreated control values, respectively. Cellular
differentiation was accompanied by down-regulation of the cytoplasmic
levels of nucleolin, a bcl-2 mRNA-stabilizing protein.
Binding of a bcl-2 mRNA instability
element (AU- rich element-1) to nucleolin in S100 extracts from
ATRA-treated cells was decreased to 15% of control within 72 h. The decay
of 5' capped, polyadenylated bcl-2 mRNA transcripts
containing ARE-1 was more rapid in S100 extracts from ATRA-treated cells

compared with untreated cells. However, when recombinant nucleolin was added to extracts of ATRA-treated cells, the rate of bcl-2 mRNA decay was similar to the rate in extracts of untreated cells. These results provide evidence that ATRA-induced apoptosis is a consequence of cellular differentiation, which leads to nucleolin down-regulation and bcl-2 mRNA instability.

L7 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2004:999715 CAPLUS
DN 141:406751
TI Assay and expression systems comprising reporter gene and instability sequence DNA for identifying compounds which affect stability of mRNA
IN Kastelic, Tania; Cheneval, Dominique
PA Novation Pharmaceuticals Inc., Can.
SO U.S. Pat. Appl. Publ., 49 pp., Cont.-in-part of U.S. Ser. No. 869,159.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2000039314	A1	20000706	WO 1999-CA1235	19991223
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CA 2603585	A1	20051013	CA 2005-2603585	20050401

WO 2005095615 A1 20051013 WO 2005-CA491
20050401
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KZ, LC,
LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ,
NA, NI,
NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK,
SL, SM,
SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU,
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PL, PT,
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GW, ML,
MR, NE, SN, TD, TG
EP 1774000 A1 20070418 EP 2005-730094
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HU, IE,
IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR
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20050401
US 20070190532 A1 20070816 US 2007-594851
20070504
PRAI GB 1998-28709 A 19981224
WO 1999-CA1235 W 19991223
US 2001-869159 A2 20010815
US 2004-814634 A 20040401
WO 2005-CA491 W 20050401

AB The present invention relates to an assay for the identification
of biol.
active compds., in particular to a reporter gene assay for the
identification of compds., which have an effect on mRNA
stability. More
particularly, the present invention relates to a reporter gene
expression
system and cell lines comprising said expression system. The
invention
further relates to compds. which destabilize mRNA. Radicicol and
radicicol analog A showed a clear effect on mRNA stability.
Human APP,
Bcl-2.alpha., c-myc, TNFα, IL-1β, VEGF
instability sequence were constructed. Instability sequence DNA
is from

The gene encoding a cytokine, a gene encoding a chemokine, a gene encoding a nuclear transcription factor, a gene encoding an oxygenase, a proto-oncogene, an immediate early gene, a cell cycle controlling gene, and a gene involved in apoptosis.

L7 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2005:208720 CAPLUS
DN 143:41672
TI Mitochondrial DNA microsatellite instability and expression of Bcl-2 and Bax mRNA in gastric cancer and its precancerous lesions
AU Fang, Dianchun; Ling, Xianlong; Luo, Yuanhui
CS Research and Treatment Center for Digestive Diseases of PLA, Southwest Hospital, Third Military Medical University, Chongqing, 400038, Peop. Rep. China
SO Jiefangjun Yixue Zazhi (2003), 28(11), 982-984
CODEN: CFCHBN; ISSN: 0577-7402
PB Jenminjun Chubanshe
DT Journal
LA Chinese
AB The relation between mitochondrial DNA microsatellite instability (mtMSI) and the expression of Bcl-2 and Bax mRNA in gastric cancer and precancerous lesions was studied. MtMSI and expression of Bcl-2 and Bax mRNA were detected with PCR-SSCP and RT-PCR, resp. Expression of Bcl-2 mRNA in intestinal metaplasia (IM, 53.3%) and dysplasia (Dys, 70%) were significantly higher than that in normal control tissue (10%), whereas no significant differences were found among chronic gastritis (CAG, 50%), gastric cancer (GC, 30%) and normal controls. Expression of Bcl-2 mRNA in Dys was higher than that in GC. Expression of Bax mRNA was significantly increased in Dys (60%), but not in CAG (50%), IM (46.7%) and GC (33.3), compared with normal control (10%). Expression of Bcl-2 and Bax mRNA in Helicobacter pylori infected gastric mucosa was significantly higher than that in non-H. pylori infected gastric mucosa, but expression of Bcl-2 and Bax mRNA were not consistent with H. pylori CagA status. MtMSI levels were 0, 10.0, 13.3, 20.0, and 36.7% in controls, CAG, IM, Dys, and GC, resp. No significant difference was found between the expression of Bcl-2 and Bax mRNA in mtMSI(+) and that in mtMSI(-) tissues. MtMSI may play an

important role in some gastric cancers, and increased mtMSI is independent
of abnormal expression of Bcl-2 and Bax mRNA.

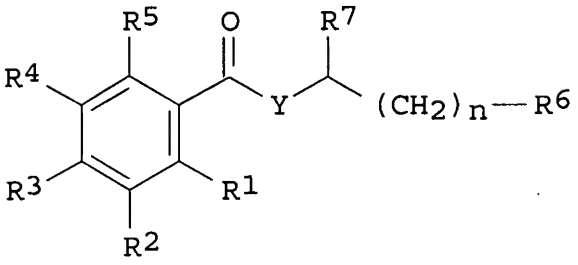
L7 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2002:240751 CAPLUS
DN 136:279323
TI Preparation of lactone-containing benzoate esters and their use as
pharmaceutical use
IN Kastelic, Tania; Cheneval, Dominique; Leutwiler, Albert
PA Novation Pharmaceuticals Inc., Can.
SO PCT Int. Appl., 57 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002024674	A1	20020328	WO 2001-CA1331	20010921
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2420185	A1	20020328	CA 2001-2420185	20010921
AU 2001093555	A	20020402	AU 2001-93555	20010921
EP 1318991	A1	20030618	EP 2001-973891	20010921
EP 1318991	B1	20060816		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004509167	T	20040325	JP 2002-529084	20010921

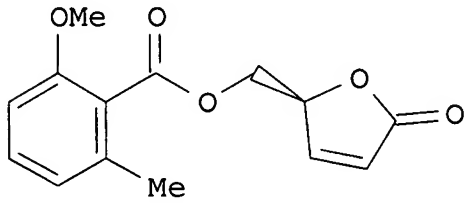
	AT 336487	T	20060915	AT 2001-973891
20010921				
	ES 2276829	T3	20070701	ES 2001-973891
20010921				
	US 20050049202	A1	20050303	US 2003-381294
20030321				
PRAI	CA 2000-2320664	A	20000921	
	WO 2001-CA1331	W	20010921	

OS MARPAT 136:279323

GI



I



II

AB The title compds. [I; R1-R5 = H, OH, halogen, (C1-4) alkyl, (C1-4) alkenyl, (C1-4) alkoxy, (C1-4) alkyl-CO2; Y = O, NR; R = H, (C1-4) alkyl; n = 0-8; R6 = 5-8-membered (un)substituted (un)saturated lactone or lactam ring; R7 = H, (C1-4) alkyl, (C1-4) alkenyl, (C1-4) alkoxy, Ph, (C1-4) alkyl-CO2], which are useful for the treatment or prevention of disorders with an etiol. associated with or comprising excessive cytokine release and are also used in the treatment of cancer, inflammatory disorders and disorders associated with an increased stability of mRNA which has an mRNA instability sequence; I-containing pharmaceutical formulation are presented. Compound II, prepared via esterification of the corresponding chiral hydroxymethyl-substituted lactone with

2-methoxy-6-methylbenzoic acid, demonstrated activity against THP-1 cell
lines.
RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> s bcl2 and AU
L8 43 BCL2 AND AU

=> dup rem l8
PROCESSING COMPLETED FOR L8
L9 36 DUP REM L8 (7 DUPLICATES REMOVED)

=> s l9 and PY<=1998
L10 5 L9 AND PY<=1998

=> d bib abs 1-
YOU HAVE REQUESTED DATA FROM 5 ANSWERS - CONTINUE? Y/(N):y

L10 ANSWER 1 OF 5 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
AN 1997:199800 BIOSIS
DN PREV199799499003
TI Peripheral blood stem cell CD34+ autologous transplant in relapsed
follicular lymphoma.
AU Marin, G. H.; Dal Cortivo, L.; Cayuela, J. M.; Marolleau, J. P.; Pautier,
P.; Cojean-Zelek, I.; Brice, P.; Makke, J.; Benbunan, M.; Gisselbrecht, C.
[Reprint author]
CS Serv. Reanimation Hematol. Adulte, Hopital Saint-Louis, 1 avenue Claude
Vellefaux, F-75475 Paris cedex 10, France
SO Hematology and Cell Therapy, (1997) Vol. 39, No. 1, pp. 33-40.
ISSN: 1269-3286.
DT Article
LA English
ED Entered STN: 12 May 1997
Last Updated on STN: 12 May 1997
AB To evaluate CD34+ selection of peripheral blood stem cells (PBSC) as a
graft for autologous transplantation. Eight relapsing follicular lymphoma
(FL) patients were submitted to CD34+ autologous stem cell transplantation
(ASCT). All patients received at least two front line conventional
therapies; mean time to treatment failure (TTF) was 4.5 months. Patients
had disseminated stage III-IV disease after a median number of 2.1

relapses. Chemotherapy and G-CSF were used as mobilization for leukapheresis. CEPRATE SC concentrator (Cell Pro, Inc, Bothell, WA) was used to select CD34+ cells from leukapheresis products. With a mean of 1.8 leukaphereses per patient, 8.1 times 10-8 mononuclear cells (MNCs)/kg were collected. After the selection process, the median number of MNCs was 9.4 times 10-6/kg; 4.3 times 10-6/kg CD34+ cells and 17 times 10-4/kg CFU-GM, with a purity of 83.7% and a viability of 89.2%. Mbr bcl2 /IgH PCR analysis of 5 grafts showed that initial buffy-coat, and CD34- fractions were negative in 3 cases and positive in 2 cases (from whom selected CD34+ fraction remained positive in 1 case). After a conditioning regimen including total body irradiation, cyclophosphamide and etoposide, CD34+ selected cells were reinfused. AU patients but one had successful engraftment, median time to WBC gt 1 times 10-9/l was 12 days and platelets gt 50 times 10-9/l 17 days. No severe infectious complications were seen. After transplant, with a minimum follow up of 2 years, 5 patients are still in complete remission (CR). Three patients have relapsed after 1 year of transplant with a mean TTF of 15.6 months. We conclude that PBSC CD34+ selection for ASCT was a safe technique, capable of reconstituting hemopoiesis without severe complications for high risk FL patients included in this study. The effects of tumor cell purging need to be evaluated in a larger series.

L10 ANSWER 2 OF 5 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
AN 1994:485444 BIOSIS
DN PREV199497498444
TI Differential induction of apoptosis in human breast tumor cells by okadaic acid and related inhibitors of protein phosphatases 1 and 2A.
AU Kiguchi, Kaoru; Glesne, David; Chubb, Cynthia H.; Fujiki, Hirota; Huberman, Eliezer [Reprint author]
CS Argonne National Lab., 9700 S. Cass Ave., Argonne, IL 60439, USA
SO Cell Growth and Differentiation, (1994) Vol. 5, No. 9, pp. 995-1004.
ISSN: 1044-9523.
DT Article

LA English
ED Entered STN: 9 Nov 1994
Last Updated on STN: 16 Dec 1994
AB To investigate a possible relationship between apoptosis induction and protein phosphorylation in human breast carcinoma cells, we treated three such cell types, MB231, MCF-7, and AU-565, with okadaic acid (OA), an inhibitor of protein phosphatases 1 and 2A, or phorbol 12 myristate 1 3-acetate, an activator of protein kinase C. We then examined these cells for the appearance of apoptosis markers. While OA caused multiplication arrest and cytotoxicity in all three cell lines, apoptosis was induced in MB-231 and MCF-7 cells but not in AU565 cells. A similar cell-specific apoptosis induction was also observed after treatment with dinophysistoxin-1 (an active OA analogue) and with calyculin A (a structurally unrelated protein phosphatase inhibitor) but not with analogues that either are inactive or penetrate epithelial cells poorly. Phorbol 12-myristate 13-acetate also inhibited cell multiplication but was without effect in inducing apoptosis in these cells. Levels of the apoptosis-inhibitory protein BCL2 were examined in these cells, but they did not correlate with this differential susceptibility. We additionally treated the three cell types with 1-beta-D-arabinofuranosylcytosine and genistein to determine whether the AU -565 cell line would also be resistant to apoptosis induction by other chemical stimuli. Both of these agents led to the induction of apoptosis in all three cell lines. These results indicate that the AU-565 cells are specifically resistant to apoptosis induction by inhibitors of protein phosphatases 1 and 2A. This cell-specific resistance may thus allow one to identify cellular mediators of apoptosis by comparing protein phosphorylation patterns in these cells before and after treatment with OA or related inhibitors.

L10 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2008 ACS on STN
AN 1996:463418 CAPLUS

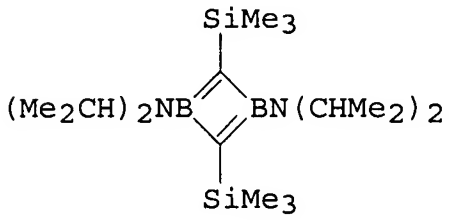
DN 125:139307
OREF 125:26029a,26032a
TI A bcl-2/IgH antisense transcript deregulates bcl-2 gene expression in human follicular lymphoma t(14:18) cell lines
AU Capaccioli, S.; Quattrone, A.; Schiavone, N.; Calastretti, A.; Copreni, E.; Bevilacqua, A.; Canti, G.; Gong, L.; Morelli, S.; Nicolin, A.
CS Inst. Gen. Pathol., Univ. Florence, Florence, 50134, Italy
SO Oncogene (1996), 13(1), 105-115
CODEN: ONCNES; ISSN: 0950-9232
PB Stockton
DT Journal
LA English
AB The 14;18 chromosome translocation, characteristic of most human follicular B-cell lymphomas, juxtaposes the bcl-2 gene with the IgH locus, creating a bcl-2/IgH hybrid gene. By mechanisms that are still under investigation, this event increases the cellular levels of the bcl-2 mRNA and thereby induces an overprodn. of the antiapoptotic BCL-2 protein which is likely responsible for neoplastic transformation. In an effort to identify potential upregulators of bcl-2 activity in t(14;18) cells, a bcl-2 antisense transcript was found by strand-specific RT-PCR that is present in the t(14;18) DOHH2 and SU-DHL-4 but not in the t(14;18)-neg. Raji and Jurkat lymphoid cell lines, and thus appears to be dependent on the bcl-2/IgH fusion. This antisense transcript is a hybrid bcl-2/IgH RNA, that originates in the IgH locus, encompasses the t(14;18) fusion site and spans at least the complete 3' UTR region of the bcl-2 mRNA. To achieve some insight into its biol. function, the t(14;18) DOHH2 cell line was treated with oligonucleotides (ODNs) by specifically targeting the bcl-2/IgH antisense strand. These ODNs lowered bcl-2 gene expression and inhibited neoplastic cell growth by inducing apoptosis. Thus, the bcl-2/IgH antisense transcript may contribute, by an unknown mechanism, to upregulation of bcl-2 gene expression in t(14;18) cells. The possibility has been considered that the hybrid antisense transcript mask AU

-rich motifs present in the 3' UTR of the bcl-2 mRNA characterized in other genes as mRNA destabilizing elements.

L10 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2008 ACS on STN
AN 1996:183430 CAPLUS
DN 124:285072
OREF 124:52719a,52722a
TI BCL-2 expression or antioxidants prevent hyperglycemia-induced formation of intracellular advanced glycation endproducts in bovine endothelial cells
AU Giardino, Ida; Edelstein, Diane; Brownlee, Michael
CS Department of Medicine, Albert Einstein College of Medicine, New York, NY, 10461, USA
SO Journal of Clinical Investigation (1996), 97(6), 1422-8
CODEN: JCINAO; ISSN: 0021-9738
PB Rockefeller University Press
DT Journal
LA English
AB Hyperglycemia rapidly induces an increase in intracellular advanced glycation end products (AGEs) in bovine endothelial cells, causing an alteration in bFGF activity. Because sugar or sugar-adduct autoxidn. is critical for AGE formation in vitro, the role of reactive oxygen species (ROS) in intracellular AGE formation was evaluated by using bovine aortic endothelial cells. Glucose (30 mM) increased intracellular ROS formation by 250% and lipid peroxidn. by 330%, while not affecting ROS in the media. In cells depleted of glutathione, intracellular AGE accumulation increased linearly with ROS generation as measured by immunoblotting and the fluorescent probe DCFH (AGE 0.258-3.531 AU* mm/5 + 104 cells, DCF 57-149 mean AU, r = 0.998, P < 0.002). Deferoxamine, α-tocopherol, and dimethylsulfoxide each inhibited hyperglycemia-induced formation of both ROS and AGE. To differentiate an effect of ROS generation on AGE formation from an effect of more distal oxidative processes, GM7373 endothelial cell lines were generated that stably expressed the peroxidn.-suppressing proto-oncogene bcl-2. Bcl-2 had no effect on hyperglycemia-induced intracellular ROS formation. In

contrast, bcl-2 expression decreased both lipid peroxidn. (100% at 3 h and
29% at 168 h) and AGE formation (55% at 168 h). These data show that a
ROS-dependent process plays a central role in the generation of
intracellular AGEs, and that inhibition of oxidant pathways prevents
intracellular AGE formation.

L10 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2008 ACS on STN
AN 1987:33148 CAPLUS
DN 106:33148
OREF 106:5567a,5570a
TI A folded and a planar 1,3-diboretane
AU Hornbach, Pia; Hildenbrand, Manfred; Pritzkow, Hans; Siebert, Walter
CS Anorg.-Chem. Inst., Univ. Heidelberg, Heidelberg, D-6900, Fed. Rep. Ger.
SO Angewandte Chemie (1986), 98(12), 1121-3
CODEN: ANCEAD; ISSN: 0044-8249
DT Journal
LA German
OS CASREACT 106:33148
GI



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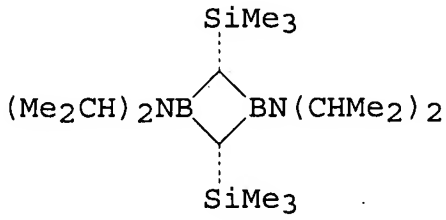
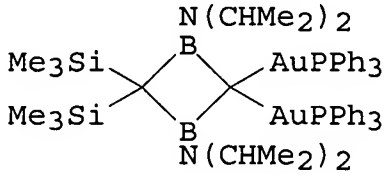


III



IV

AB Treatment of B2Cl4 with Me3SiC.tplbond.CSiMe3 gave (Me3Si)2C:C(BCl2)2 which was treated with (Me2CH)2NH to give
(Me3Si)2C:C[BClN(CHMe2)2]2. Treatment of the latter compound with NaK8 gave
the diborate I which gave a stable dianion (II) by treatment with more
NaK8. Hydrogenation of I gave the diboretane III which was also obtained
by treating II with CHCl3 or HN(SiNe3)2. Treatment of II with Ph3PAuCl

gave the Au derivative IV.

```
=> FIL STNGUIDE
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                      ENTRY    SESSION
FULL ESTIMATED COST                                    54.54     96.21

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                      ENTRY    SESSION
CA SUBSCRIBER PRICE                                    -4.80
-7.20

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=> FIL BIOSIS CAPLUS EMBASE
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                      ENTRY    SESSION
FULL ESTIMATED COST                                     0.06     96.27

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                      ENTRY    SESSION
CA SUBSCRIBER PRICE                                     0.00
-7.20

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=> d his

     (FILE 'HOME' ENTERED AT 15:24:37 ON 02 SEP 2008)

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L2           964 S MRNA (3A) INSTABIL?
L3             0 S L1 AND APP
L4             3 S L2 AND APP
L5             3 DUP REM L4 (0 DUPLICATES REMOVED)
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     FILE 'BIOSIS, CAPLUS, EMBASE' ENTERED AT 15:41:06 ON 02 SEP 2008
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L7             6 DUP REM L6 (4 DUPLICATES REMOVED)
L8            43 S BCL2 AND AU
L9            36 DUP REM L8 (7 DUPLICATES REMOVED)
L10            5 S L9 AND PY<=1998

     FILE 'STNGUIDE' ENTERED AT 15:49:29 ON 02 SEP 2008

     FILE 'BIOSIS, CAPLUS, EMBASE' ENTERED AT 15:49:55 ON 02 SEP 2008

=> s BCL 2 and (ARE or AU)
L11       28853 BCL 2 AND (ARE OR AU)

=> FIL STNGUIDE
COST IN U.S. DOLLARS                                  SINCE FILE      TOTAL
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FULL ESTIMATED COST                                      11.53     107.80

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)            SINCE FILE      TOTAL
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CA SUBSCRIBER PRICE                                       0.00
-7.20

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FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Aug 29, 2008 (20080829/UP).

=> FIL BIOSIS CAPLUS EMBASE
COST IN U.S. DOLLARS                                  SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                       0.36     108.16

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)            SINCE FILE      TOTAL
                                                         ENTRY    SESSION
CA SUBSCRIBER PRICE                                       0.00
-7.20

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FILE 'CAPLUS' ENTERED AT 15:56:07 ON 02 SEP 2008
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FILE 'EMBASE' ENTERED AT 15:56:07 ON 02 SEP 2008
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=> s AU (3a) rich
L12       3839 AU (3A) RICH

=> s l12 and BCL 2
L13         57 L12 AND BCL 2

=> s l13 and py<=1998
L14          3 L13 AND PY<=1998

=> dup rem l14
PROCESSING COMPLETED FOR L14
L15           1 DUP REM L14 (2 DUPLICATES REMOVED)

=> d bib abs

L15  ANSWER 1 OF 1  BIOSIS  COPYRIGHT (c) 2008 The Thomson
Corporation  on STN
     DUPLICATE 1
AN   1996:414837  BIOSIS
DN   PREV199699137193
TI   A bcl-2/IgH antisense transcript deregulates
     bcl-2 gene expression in human follicular lymphoma
     t(14;18) cell lines.
AU   Capaccioli, S.; Quattrone, A.; Schiavone, N.; Calastretti, A.;
Copreni,
     E.; Bevilacqua, A.; Canti, G.; Gong, L.; Morelli, S.; Nicolin,
A. [Reprint
     author]
CS   Dep. Pharmacol., Sch. Med., Via Vanvitelli 32, 20129 Milan, Italy
SO   Oncogene, (1996) Vol. 13, No. 1, pp. 105-115.
     CODEN: ONCNES. ISSN: 0950-9232.
DT   Article
LA   English
ED   Entered STN: 10 Sep 1996
     Last Updated on STN: 10 Sep 1996
AB   The 14;18 chromosome translocation, characteristic of most human
     follicular B-cell lymphomas, juxtaposes the bcl-2 gene
     with the IgH locus, creating a bcl-2/IgH hybrid gene.
     By mechanisms that are still under investigation, this event
increases the
     cellular levels of the bcl-2 mRNA and thereby induces
     an overproduction of the antiapoptotic BCL-2 protein
     which is likely responsible for neoplastic transformation.  In
an effort
     to identify potential upregulators of bcl-2 activity
     in t(14;18) cells, we found, by strand-specific RT-PCR, a hcl-2
antisense
     transcript that is present in the t(14;18) DOHH2 and SU-DHL-4
but not in
     the t(14;18)-negative Raji and Jurkat lymphoid cell lines, and
thus
```

appears to be dependent on the bcl-2/IgH fusion. This antisense transcript is a hybrid bcl-2/IgH RNA, that originates in the IgH locus, encompasses the t(14;18) fusion site and spans at least the complete 3' UTR region of the bcl-2 mRNA. To achieve some insight into its biological function, we treated the t(14;18) DOHH2 cell line with oligonucleotides (ODNs) by specifically targeting the bcl-2/IgH antisense strand. These ODNs lowered bcl-2 gene expression, inhibited neoplastic cell growth by inducing apoptosis. We would like to propose the hypothesis that the bcl-2/IgH antisense transcript may contribute, by an unknown mechanism, to upregulation of bcl-2 gene expression in t(14;18) cells. The possibility has been considered that the hybrid antisense transcript mask AU-rich motifs present in the 3' UTR of the bcl-2 mRNA characterized in other genes as mRNA destabilizing elements.

=> FIL STNGUIDE

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	16.95	125.11

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	

-7.20

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LAST RELOADED: Aug 29, 2008 (20080829/UP).

=> FIL BIOSIS CAPLUS EMBASE

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.06	125.17

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	

-7.20

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FILE 'EMBASE' ENTERED AT 15:58:39 ON 02 SEP 2008

=> s mRNA (3a) stabil?
L16 18718 MRNA (3A) STABIL?

=> s l16 and bcl 2
L17 120 L16 AND BCL 2

=> s l17 and pY<=1998
L18 10 L17 AND PY<=1998

=> dup rem l18
PROCESSING COMPLETED FOR L18
L19 5 DUP REM L18 (5 DUPLICATES REMOVED)

=> d bib abs 1-
YOU HAVE REQUESTED DATA FROM 5 ANSWERS - CONTINUE? Y/(N):y

L19 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2008 ACS on STN
AN 1998:672675 CAPLUS
DN 129:271496
OREF 129:55245a,55248a
TI Viral vectors for identification of RNA regulatory sequences and interacting molecules
IN Blau, Helen M.; Spicher, Albert; Guicherit, Oivin
PA The Board of Trustees of the Leland Stanford Junior University, USA
SO PCT Int. Appl., 64 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9842854	A1	19981001	WO 1998-US6093	19980327 <--

W: CA, JP
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
PRAI US 1997-42543P P 19970327
AB Methods and compns. for the identification, characterization and isolation of regulatory RNA sequences are provided. Regulatory RNA sequences mediate post-transcriptional regulation in response to various environmental conditions and can be used to alter the level of expression

of endogenous genes or to identify factors which interact with regulatory RNA sequences. The invention addnl. provides improved vector systems for rapid screening, anal., and tightly-regulated expression of regulatory RNA sequences. The regulatory properties of highly conserved regions (HCRs) within 3'-UTRs that have retained greater than 70% homol. within stretches of 100 nucleotides over 30 million years were examined A retroviral vector system was used with a selectable marker that allowed rapid delivery of 3'-UTR-reporter constructs to populations of thousands of cells within one to two weeks, avoiding problems associated with clonal anal. and long-term selection. Addnl., this vector is modular, thereby permitting direct comparison of different HCRs on gene expression, independent of 5'-UTRs, promoters, protein coding regions and polyadenylation signals. Ten HCRs (from c-fos, c-myc, transferrin receptor, bcl2, EF1α, vimentin, ornithine decarboxylase, fibronectin, HuD and Ran genes) were examined Nine of these HCRs (i.e., all except the Ran HCR) were found to decrease mRNA stability to different extents. Two HCRs (the c-fos and vimentin HCRs) altered mRNA translation under steady-state conditions. Four HCRs (the HuD, Ran, fibronectin and ornithine decarboxylase HCRs) mediated responses to changes in mitogen level by increasing reporter protein levels 2-fold while 2 HCRs exhibited a 6-fold difference in their response to another environmental stress, hypoxia.

RE.CNT 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 2 OF 5 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
DUPLICATE 1
AN 1997:160160 BIOSIS
DN PREV199799459363
TI Increased gadd153 messenger RNA level is associated with apoptosis in human leukemic cells treated with etoposide.
AU Eymin, Beatrice; Dubrez, Laurence; Allouche, Michele; Solary, Eric

[Reprint author]
CS Lab. Oncohematol. Pharmacol., CJF INSERM 94-08, UFR Med./Pharmacy, 7
boulevard Jeanne d'Arc, 21033 Dijon, France
SO Cancer Research, (1997) Vol. 57, No. 4, pp. 686-695.
CODEN: CNREA8. ISSN: 0008-5472.
DT Article
LA English
ED Entered STN: 15 Apr 1997
Last Updated on STN: 15 Apr 1997
AB Treatment of leukemic cells with topoisomerase inhibitors can lead to growth arrest and subsequent apoptotic cell death. The relationships between cell cycle regulation and apoptosis triggering remain poorly understood. The gadd153 gene encodes the nuclear protein CHOP 10 that acts as a negative modulator of CCAAT/enhancer binding protein transcriptional factors and inhibits cell cycle progression. We have investigated the relationships between gadd153 gene expression and apoptosis induction in four human leukemic cell lines with different sensitivities to apoptosis induced by etoposide (VP-16), a topoisomerase 11 inhibitor. The gadd153 gene was constitutively expressed in the four studied cell lines. In U937 and HL-60 cells that were very sensitive to apoptosis induction by the drug, VP-16 induced a time- and dosedependent increase of gadd153 gene mRNA expression. Using agarose gel electrophoresis and a quantitative filter elution assay, apoptotic DNA fragmentation was observed to begin when gadd153 gene expression increased. Equitoxic doses of VP-16 (as defined using a 96-h 3-4,5-dimethylthiazol-2,5-diphenyltetrazolium bromide assay) did not increase the gadd153 mRNA level in K562 and KCL22 cell lines that were more resistant to apoptosis induction by the drug. Nuclear run-on and mRNA stability experiments demonstrated that VP-16 treatment increased gadd153 gene transcription in the sensitive U937 cells. Cycloheximide did not prevent gadd153 expression increase. Both gadd153 mRNA level increase and internucleosomal DNA fragmentation were inhibited by N-tosyl-L-phenylalanine chloromethylketone, a serine

threonine protease inhibitor, N-acetyl-leucyl-leucyl-norleucinal, an inhibitor of calpain, N-acetylcysteine, an inhibitor of oxidative metabolism, and overexpression of Bcl-2. Z-VAD and Z-DEVD peptides that inhibit interleukin 1-beta-converting enzyme-like proteases suppressed DNA fragmentation without preventing gadd153 mRNA increase in VP-16-treated U937 cells. These results indicate that gadd153 gene expression increase occurs downstream of events sensitive to N-tosyl-L-phenylalanine chloromethylketone, calpain inhibitor I, and Bcl-2 and upstream of interleukin 1-beta-converting enzyme-related proteases activation in leukemic cells in which treatment with VP-16 induces rapid apoptosis.

L19 ANSWER 3 OF 5 EMBASE

AN 1997289087 EMBASE

TI Dexamethasone suppresses apoptosis in a human gastric cancer cell line through modulation of bcl-x gene expression.

AU Chang, Tsu-Chung (correspondence); Chu, Jing-Tsai; Chu, Li-Ling

CS Department of Biochemistry, Natl. Def. Med. Ctr., P.O. B., Taipei, Taiwan, Province of China.

AU Hung, Mei-Whey; Tsai, Lai-Chen

CS Department of Medical Research, Veterans General Hospital, Taipei, Taiwan, Province of China.

AU Jiang, Shu-Yang

CS Grad. Institute of Medical Sciences, National Defense Medical Center, Taipei, Taiwan, Province of China.

AU Chang, Tsu-Chung (correspondence)

CS Department of Biochemistry, National Defence Medical Center, PO Box 90048-501, Taipei, Taiwan, Province of China.

SO FEBS Letters, (22 Sep 1997) Vol. 415, No. 1, pp. 11-15.
Refs: 26
ISSN: 0014-5793 CODEN: FEBLAL

PUI S 0014-5793(97)01083-1

CY Netherlands

DT Journal; Article

FS 016 Cancer
029 Clinical and Experimental Biochemistry
037 Drug Literature Index

LA English

SL English

ED Entered STN: 9 Oct 1997
Last Updated on STN: 9 Oct 1997
AB Treatment of human gastric cancer TMK-1 cells with transcription and translation inhibitors rapidly triggered cell apoptosis. Along with cell apoptosis, the Bcl-x(S) level was markedly upregulated suggesting a crucial role of this protein in promoting tile apoptotic process. In the presence of dexamethasone, however, cell apoptosis was greatly attenuated as demonstrated by DNA histogram shift and DNA fragmentation. Studies using the glucocorticoid receptor antagonist RU486 indicated that attenuation of apoptosis was mediated through glucocorticoid receptors. Dexamethasone not only suppressed the apoptosis-associated upregulation of Bcl-x(S) but also enhanced the basal level of Bcl-x(L) in the cells. In addition, bcl-x mRNA stability was significantly extended in the presence of dexamethasone, These results indicate that dexamethasone exerted a protective effect and delayed apoptosis of TMK-1 cells by modulating bcl-x gene expression.

L19 ANSWER 4 OF 5 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
DUPLICATE 2
AN 1997:42737 BIOSIS
DN PREV199799334725
TI Modulation of apoptosis-associated genes bcl-2, bcl-x, and bax during rat liver regeneration.
AU Kren, Betsy T.; Trembley, Janeen H.; Krajewski, Stanislaw; Behrens, Timothy W.; Reed, John C.; Steer, Clifford J. [Reprint author]
CS Dep. Med., Univ. Minnesota Med. Sch., Box 36 UMHC, 516 Delaware Street SE, Minneapolis, MN 55455, USA
SO Cell Growth and Differentiation, (1996) Vol. 7, No. 12, pp. 1633-1642.
ISSN: 1044-9523.
DT Article
LA English
ED Entered STN: 28 Jan 1997
Last Updated on STN: 28 Jan 1997
AB Liver regeneration (LR) after 70% partial hepatectomy (pH) represents a unique in vivo model of cell cycle and gene regulation. This study was

conducted to characterize apoptosis-associated gene expression during LR.
The results indicated that transcripts for both bcl-x and bcl-2 exhibited similar patterns of expression during LR with peaks at 6 h post-PH. In contrast, the major 1.1-kb bax transcript exhibited peaks at 18 (P lt 0.05) and 72 h (P lt 0.001) post-PH. Nuclear run-on analyses for all three genes indicated no detectable transcription rate changes during LR. At 6 h post-PH, when bcl-x mRNA levels were increased by 25-fold (P lt 0.001), bcl-x mRNA half-life was elevated 4-fold (P lt 0.001). Similarly, bax transcript half-life increased from 2.8 h at 0 h to 4.3 h at 24 h (P lt 0.001) and gt 8 h at 40 h (P lt 0.001) post-PH, coincident with increases in steady-state levels of mRNA. Western blot analyses of Bcl-2 and Bcl-x proteins showed no significant change through 96 h of LR, whereas Bax protein levels cycled in parallel with its mRNA. Interestingly, novel Bax- and Bcl-2-cross-reactive proteins of 31 and 32 kDa, respectively, were detected in nuclei isolated from quiescent liver. When liver growth was induced by the peroxisome proliferator clofibrate, transcript and protein levels were coupled for bcl-x but not for bax. In conclusion, the apoptosis-associated genes bcl-2, bcl-x and bax are modulated at the transcript and protein levels during LR, suggesting a role for these gene products in normal liver growth. The alterations in transcript levels occur posttranscriptionally and involve changes in mRNA stability. Furthermore, unlike bax, steady-state protein and transcript levels are uncoupled for both bcl-2 and bcl-x, suggesting a role for translational regulation during LR after PH.

L19 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2008 ACS on STN DUPLICATE 3
AN 1989:592378 CAPLUS
DN 111:192378
OREF 111:31935a,31938a
TI Regulation of bcl-2 gene expression in lymphoid cell lines containing normal #18 or t(14;18) chromosomes
AU Reed, John C.; Tsujimoto, Yoshihide; Epstein, Scott F.; Cuddy, Michael;

Slabiak, Trina; Nowell, Peter C.; Croce, Carlo M.
CS Sch. Med., Univ. Pennsylvania, Philadelphia, PA, 19104-6082, USA
SO Oncogene Research (1989), 4(4), 271-82
CODEN: ONCGE7; ISSN: 0890-6467
DT Journal
LA English
AB The bcl-2 (B cell lymphoma/leukemia-2) gene at band 18q21 is involved in t(14;18) chromosomal translocations in most follicular lymphomas and occasional other human B cell malignancies, where it becomes juxtaposed to the transcriptionally active Ig (Ig) locus at 14q32. Regulation of bcl-2 gene expression was investigated in neoplastic lymphoid cell lines containing normal #18 chromosomes or a t(14;18) translocation with regard to steady-state mRNA levels, RNA stability, transcription rates, and DNA methylation. High steady-state levels of bcl-2 mRNA, and proportionally high rates of bcl-2 transcription (measured in isolated nuclei), were found in B cell lines containing t(14;18) translocations. The half-life of bcl-2 mRNA was similar in all cell lines examined, including a t(14;18)-containing follicular lymphoma cell line, which has a translocated and rearranged bcl-2 gene that produces bcl-2/Ig fusion transcripts. However, in the presence of cycloheximide (inhibitor of protein synthesis), the half-life of some of the bcl-2 /Ig mRNAs produced by these cells was prolonged, indicating that in some circumstances mRNA stability may contribute to deregulated bcl-2 expression. Despite stabilizing some bcl-2 mRNAs, the overall effect of treating cell lines with cycloheximide was a reduction in the levels of accumulated bcl-2 mRNAs through inhibition of bcl-2 gene transcription. These latter data provide indirect evidence that short-lived transacting factor(s) regulate transcription of the human bcl-2 gene in lymphoid cells with or without a t(14;18) translocation. No clear correlation was discovered between bcl-2 gene methylation and transcription.

=> s bcl 2 alpha
L20 154 BCL 2 ALPHA

=> s l20 and ARE
L21 56 L20 AND ARE

=> dup rem l21
PROCESSING COMPLETED FOR L21
L22 36 DUP REM L21 (20 DUPLICATES REMOVED)

=> d bib abs 1-
YOU HAVE REQUESTED DATA FROM 36 ANSWERS - CONTINUE? Y/(N):y

L22 ANSWER 1 OF 36 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2007:1116179 CAPLUS
DN 147:462499
TI Activation of melanocortin 4 receptors reduces the inflammatory response
and prevents apoptosis induced by lipopolysaccharide and interferon-γ in astrocytes
AU Caruso, Carla; Durand, Daniela; Schioth, Helgi B.; Rey, Rodolfo; Seilicovich, Adriana; Lasaga, Mercedes
CS Centro de Investigaciones en Reproduccion, School of Medicine, University
of Buenos Aires, Buenos Aires, 1121ABG, Argent.
SO Endocrinology (2007), 148(10), 4918-4926
CODEN: ENDOAO; ISSN: 0013-7227
PB Endocrine Society
DT Journal
LA English
AB α-MSH exerts an immunomodulatory action in the brain and may play a
neuroprotective role acting through melanocortin 4 receptor (MC4Rs). In
the present study, we show that MC4Rs are constitutively
expressed in astrocytes as determined by immunocytochem., RT-PCR, and Western
blot anal. α-MSH (5 μM) reduced the nitric oxide production and the
expression of inducible nitric oxide synthase (iNOS) induced by bacterial
lipopolysaccharide (LPS, 1 μg/mL) plus interferon-γ (IFN-γ,
50 ng/mL) in cultured astrocytes after 24 h. α-MSH also attenuated
the stimulatory effect of LPS/IFN-γ on prostaglandin E2 release and
cyclooxygenase-2 (COX-2) expression. Treatment with HS 024, a selective
MC4R antagonist, blocked the antiinflammatory effects of α-MSH,
suggesting a MC4R-mediated mechanism in the action of this melanocortin.
In astrocytes, LPS/IFN-γ treatment reduced cell viability, increased
the number of terminal deoxynucleotidyl transferase-mediated dUTP nick-end
labeling-pos. cells and activated caspase-3. α-MSH prevented these

apoptotic events, and this cytoprotective effect was abolished by HS 024.
LPS/IFN-γ decreased Bcl-2, whereas it increased Bax protein expression in astrocytes, thus increasing the Bax/Bcl-2 ratio.
α-MSH produced a shift in Bax/Bcl-2 ratio toward astrocyte survival
because it increased Bcl-2 expression and also prevented the effect of
LPS/IFN-γ on Bax and Bcl-2 expression. In summary, these findings
suggest that α-MSH, through MC4R activation, attenuates
LPS/IFN-γ-induced inflammation by decreasing iNOS and COX-2
expression and prevents LPS/IFN-γ-induced apoptosis of astrocytes by
modulating the expression of proteins of the Bcl-2 family.
RE.CNT 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 2 OF 36 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2007:812134 CAPLUS
DN 148:97655
TI Alpha-fetoprotein-specific transfer factors downregulate alpha-fetoprotein
expression and specifically induce apoptosis in Bel7404
alpha-fetoprotein-positive hepatocarcinoma cells
AU Zhang, Hui; Bai, Zengliang; Chen, Jing; Wang, Ze; Li, Juan
CS School of Life Science, Shandong University, Jinan, Peop. Rep. China
SO Hepatology Research (2007), 37(7), 557-567
CODEN: HPRSFM; ISSN: 1386-6346
PB Blackwell Publishing Asia Pty Ltd.
DT Journal
LA English
AB Aim: To investigate the mechanisms of AFP-specific transfer factors
(AFP-TF) in induced Bel7402 cells apoptosis. Further, we investigate the
interaction between AFP-TF and AFP in the apoptosis. Methods: Bel7402 and
HepG2 AFP-pos. hepatocarcinoma cell lines, SK-Hep-1 AFP-neg.
hepatocarcinoma cell line and Changliver normal liver cell line
are used. Cell viability is evaluated by MTT assay and apoptosis
is measured by Hoechst33342 staining and TUNEL assay. FACS is used to
analyze the cell cycle. AFP expression is examined by RT-PCR, Western
blotting and immunocytochem. The interaction between AFP-TF and AFP in
the apoptosis is investigated by addition of AFP in cultures or AFP
transfection in Bel7402 cells prior to AFP-TF treatment. Mitochondrial

membrane potential (ΔΨm) and intracellular Ca2+ concentration are resp. measured by Rhodamine123 and Fluo-3 AM Ester. Western blotting detects the involvement of several apoptosis-related proteins.
Finally, caspase-3 and Caspase-9 activity are resp. examined
Results: AFP-TF can induce apoptosis in Bel7402 and HepG2 AFP-pos.
hepatocarcinoma cells, but not SK-Hep-1 and Changliver cells. AFP-mRNA
level changes little in apoptotic Bel7402 cells; while AFP expression is
downregulated and uniformly dispersed throughout the whole cell. Addition of
exogenous AFP or overexpression of intracellular AFP can reduce such
apoptotic effect. Besides, apoptotic Bel7402 cells show a disruption of
ΔΨm, an immediate elevation of Ca2+ concentration, a prominently
decreased ratio of bcl-2 to bax, a release of cytochrome c from
mitochondria to cytosol, and ultimately an activation of caspase-9 and
caspase-3. Conclusion: AFP-TF induced Bel7402 cells apoptosis is
mitochondrial-dependent and is mediated by the interaction of AFP-TF with
intracellular AFP.
RE.CNT 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 3 OF 36 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2006:1316230 CAPLUS
DN 146:200431
TI (α/β+α)-Peptide Antagonists of BH3 Domain/Bcl-xL
Recognition: Toward General Strategies for Foldamer-Based Inhibition of
Protein-Protein Interactions
AU Sadowsky, Jack D.; Fairlie, W. Douglas; Hadley, Erik B.; Lee, Hee-Seung;
Umezawa, Naoki; Nikolovska-Coleska, Zaneta; Wang, Shaomeng; Huang, David
C. S.; Tomita, York; Gellman, Samuel H.
CS Department of Chemistry, University of Wisconsin, Madison, WI, 53706, USA
SO Journal of the American Chemical Society (2007), 129(1), 139-154
CODEN: JACSAT; ISSN: 0002-7863
PB American Chemical Society
DT Journal
LA English
OS CASREACT 146:200431
AB The development of mols. that bind to specific protein surface sites and
inhibit protein-protein interactions is a fundamental challenge in mol.

recognition. New strategies for approaching this challenge could have important long-term ramifications in biol. and medicine. We are exploring the concept that unnatural oligomers with well-defined conformations ("foldamers") can mimic protein secondary structural elements and thereby block specific protein-protein interactions. Here, we describe the identification and anal. of helical peptide-based foldamers that bind to a specific cleft on the anti-apoptotic protein Bcl-xL by mimicking an α-helical BH3 domain. Initial studies, employing a fluorescence polarization (FP) competition assay, revealed that among several α/β- and β-peptide foldamer backbones only α/β-peptides intended to adopt 14/15-helical secondary structure display significant binding to Bcl-xL. The most tightly binding Bcl-xL ligands are chimeric oligomers in which an N-terminal α/β-peptide segment is fused to a C-terminal α-peptide segment ((α/β+α)-peptides). Sequence-affinity relationships were probed via standard and nonstandard techniques (alanine scanning and hydrophile scanning, resp.), and the results allowed us to construct a computational model of the ligand/Bcl-xL complex. Anal. ultracentrifugation with a high-affinity (α/β+α)-peptide established 1:1 ligand:Bcl-xL stoichiometry under FP assay conditions. Binding selectivity studies with the most potent (α/β+α)-peptide, conducted via surface plasmon resonance measurements, revealed that this ligand binds tightly to Bcl-w as well as to Bcl-xL, while binding to Bcl-2 is somewhat weaker. No binding could be detected with Mcl-1. We show that our most potent (α/β+α)-peptide can induce cytochrome C release from mitochondria, an early step in apoptosis, in cell lysates, and that this activity is dependent upon inhibition of protein-protein interactions involving Bcl-xL.
RE.CNT 88 THERE ARE 88 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 4 OF 36 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2005:1055893 CAPLUS
DN 143:403736
TI Activation of caspase 8 in the pituitaries of streptozotocin-induced diabetic rats: Implication in increased apoptosis of lactotrophs

AU Arroba, Ana I.; Frago, Laura M.; Argente, Jesus; Chowen, Julie A.
CS Hospital Infantil Universitario Nino Jesus, Universidad Autonoma, Department of Endocrinology, Madrid, 28009, Spain
SO Endocrinology (2005), 146(10), 4417-4424
CODEN: ENDOAO; ISSN: 0013-7227
PB Endocrine Society
DT Journal
LA English
AB Lactotroph cell death is increased in streptozotocin-induced diabetic rats. To determine the mechanism involved, cell death proteins were accessed in pituitaries of diabetic (streptozotocin at 65 mg/kg, 2 mo evolution) and control male rats by Western blot anal. and double immunohistochem. The intact and cleaved forms of caspase 9 were increased in diabetic rat pituitaries compared with controls. Although the proforms of caspases 3, 6, and 7 were increased in diabetic rat pituitaries, their activated forms were either unchanged or decreased. Activation of these effector caspases may be blocked by the increased expression of X-chromosome-linked inhibitor of apoptosis protein (XIAP) in diabetic rat pituitaries. However, in diabetic rats, XIAP expression in lactotrophs was decreased, suggesting that this cell type is not protected. Caspase 8, p53, and nuclear factor κB were more highly activated in diabetic rat pituitaries, with caspase 8 colocalization in lactotrophs being increased. These results suggest that, in the pituitaries of diabetic rats, the cascades of normal cell turnover are partially inhibited, possibly via XIAP, and this may be cell specific. Furthermore, activation of the extrinsic cell-death pathway, including activation of caspase 8, may underlie the diabetes-associated increase in lactotroph death.
RE.CNT 56 THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 5 OF 36 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2005:430555 CAPLUS
DN 142:476527
TI α-Melanocortin and endothelin-1 activate antiapoptotic pathways and reduce DNA damage in human melanocytes

AU Kadekaro, Ana Luisa; Kavanagh, Renny; Kanto, Hiromi; Terzieva, Silva;
Hauser, Jennifer; Kobayashi, Nobuhiko; Schwemberger, Sandy; Cornelius,
James; Babcock, George; Shertzer, Howard G.; Scott, Glynis; Abdel-Malek,
Zalfa A.
CS Department of Dermatology, University of Cincinnati College of Medicine
and Shriners' Burns Institute, Cincinnati, OH, USA
SO Cancer Research (2005), 65(10), 4292-4299
CODEN: CNREA8; ISSN: 0008-5472
PB American Association for Cancer Research
DT Journal
LA English
AB UV radiation is an important etiol. factor for skin cancer, including
melanoma. Constitutive pigmentation and the ability to tan are considered the main photoprotective mechanism against sun-induced carcinogenesis. Pigmentation in the skin is conferred by epidermal
melanocytes that synthesize and transfer melanin to keratinocytes.
Therefore, insuring the survival and genomic stability of epidermal
melanocytes is critical for inhibiting photocarcinogenesis, particularly
melanoma, the most deadly form of skin cancer. The paracrine factors
α-melanocortin and endothelin-1 are critical for the melanogenic response of cultured human melanocytes to UV radiation. The
authors report that α-melanocortin and endothelin-1 rescued human
melanocytes from UV radiation-induced apoptosis and reduced DNA photoproducts and oxidative stress. The survival effects of α-melanocortin and endothelin-1 were mediated by activation of the
melanocortin 1 and endothelin receptors, resp. Treatment of melanocytes
with α-melanocortin and/or endothelin-1 before exposure to UV radiation activated the inositol triphosphate kinase-Akt pathway and
increased the phosphorylation and expression of the microphthalmia-related
transcription factor. Treatment with α-melanocortin and/or endothelin-1 enhanced the repair of cyclobutane pyrimidine dimers and
reduced the levels of hydrogen peroxide induced by UV radiation. These
effects are expected to reduce genomic instability and mutagenesis.

RE.CNT 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 6 OF 36 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2005:1000002 CAPLUS
DN 143:318603
TI α-Tocopheryl succinate selectively induces apoptosis in neuroblastoma cells: Potential therapy of malignancies of the nervous system?
AU Swettenham, Emma; Witting, Paul K.; Salvatore, Brian A.; Neuzil, Jiri
CS Apoptosis Research Group, School of Medical Science, Griffith University, Southport, Queensland, Australia
SO Journal of Neurochemistry (2005), 94(5), 1448-1456
CODEN: JONRA9; ISSN: 0022-3042
PB Blackwell Publishing Ltd.
DT Journal
LA English
AB Vitamin E (VE) analogs, epitomized by α-tocopheryl succinate (α-TOS), are potent inducers of apoptosis and anti-cancer agents. Here, we tested their effect on the highly malignant N-type neuroblastoma (Nb) cells and their differentiated, neuron-like counterparts. Nb cells were highly susceptible to several VE analogs, while differentiated Nb cells were relatively resistant to α-TOS. The importance of caspase-9 rather than caspase-8, as judged by specific siRNAs studies, together with the loss of the inner mitochondrial potential, suggests that α-TOS triggers apoptosis in Nb cells via the mitochondrial pathway. Cultured Nb cells were sensitized to α-TOS by pre-treatment with Bcl-2, Bcl-xL or Mcl-1 siRNAs, while the malignant cell line was more resistant to the vitamin E analog when Bax was knocked down. In contrast, overexpression of Bcl-2 in Nb cells rendered them more resistant to α-TOS-induced apoptosis. The resistance of differentiated Nb cells to α-TOS-mediated apoptosis occurred via two modes: first, by up-regulation of the anti-apoptotic Bcl-2 family proteins and second, by accumulation of decreased levels of reactive oxygen species when challenged with α-TOS. We conclude that α-TOS is highly selective in killing malignant brain cancer cells while relatively inert toward differentiated neuronal cells, and

that vitamin E analogs may be novel therapeutics for the treatment of tumors such as neuroblastomas.

RE.CNT 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 7 OF 36 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2005:781625 CAPLUS
DN 143:343592
TI α5β1 Integrin stimulates Bcl-2 expression and cell survival through Akt, focal adhesion kinase, and Ca2+/calmodulin-dependent protein kinase IV
AU Lee, Byung-Heon; Ruoslahti, Erkki
CS Department of Biochemistry and Research Institute for Cell & Matrix Biology, School of Medicine, Kyungpook National University, Taegu, 700-422, S. Korea
SO Journal of Cellular Biochemistry (2005), 95(6), 1214-1223
CODEN: JCEBD5; ISSN: 0730-2312
PB Wiley-Liss, Inc.
DT Journal
LA English
AB CHO cells expressing α5β1 integrin are more resistant to apoptosis and express more Bcl-2 than the same cells engineered to express αvβ1 or cytoplasmically truncated α5Δcβ1 integrin as their main fibronectin receptor. The Bcl-2 up-regulation by α5β1 is mediated, at least in part, by the focal adhesion kinase (FAK) and phosphatidylinositol-3 kinase (PI3K)/Akt pathways. Here, we show that integrin-mediated activation of Ca2+/calmodulin-dependent protein kinase (CaMK) IV, and the NF-κB and CREB transcription factors also enhance the integrin-dependent regulation of Bcl-2 expression in the α5β1 cells. A forkhead transcription factor, which is inactivated Akt, blocked Bcl-2 expression. The FAK pathway was found to be defective in both the αvβ1 and α5Δcβ1 cells. These cell lines differed from one another in 2 Bcl-2-regulating pathways: adhesion through αvβ1 failed to activate Akt, allowing forkhead to suppress Bcl-2 transcription, whereas α5Δcβ1 did not activate NF-κB and CREB, presumably because CaMK IV was not activated. Our results indicate that 3 pathways, the FAK, PI3K/Akt, and CaMK IV mediate the survival-supporting activity of α5β1 integrin.

RE.CNT 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 8 OF 36 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
DUPLICATE 1
AN 2005:235197 BIOSIS
DN PREV200510021601
TI Diagnostic challenge of fetal ontogeny and its application on the ovarian
teratomas.
AU Cho, Nam Hoon [Reprint Author]; Kim, Young Tae; Lee, Ji-Hwan; Song,
Chanil; Cho, Sung-Woo; Cho, Sang Ho; Chi, Je Geun
CS Yonsei Univ, Coll Med, Dept Pathol, Brain Korea 21 Project Med Sci,
Shinchon Dong 134, Seoul 120752, South Korea
SO International Journal of Gynecological Pathology, (APR 2005) Vol. 24, No.
2, pp. 173-182.
ISSN: 0277-1691.
DT Article
LA English
ED Entered STN: 23 Jun 2005
Last Updated on STN: 23 Jun 2005
AB Although neuroepithelial tubules (NET) often are a component of immature teratoma (IT), they are not always required for diagnosis. Other somatic elements are sufficient and often verified with immunnohistochemical stain. This study was designed to determine the definition of immaturity versus fetal ontogeny, using several molecular markers in IT. It is our contention that IT is equivalent to an embryonic stage less than a fertilization age (FA) of 8 weeks, and a mature teratoma (MT) to a fetal stage later than a FA of 8 weeks, whereas an embryonal carcinoma (Eca) matches a pre-embryonic stage earlier than a FA of 2 weeks. The teratomatous components used as a roadmap to evaluate maturity included: a lobular structure of primitive endodermal tubules (FA 4 14 to 6 weeks), a ventricle-lined cortical plate (FA 9 weeks), a complex papillary choroid plexus (FA 10 weeks), melanin deposition in hair follicles (FA 15 weeks), and the bell stage of odontogenesis (FA 19 weeks). The teratomatous components of 25 resected ovarian solid teratoma samples were compared with fetal ontogeny. For an inimuno-histochemical analysis, the CD30, CD34, CD99, bcl-

2, alpha-fetoprotein (AFP), and placenta-like alkaline phosphatase (PLAP) were assessed. The AFP and Ki-1 were positive in the embryoid body, which was identified at a FA less than 4 weeks in Eca. The AFP was positive in the primitive endodermal components and some of the squamous epithelium in IT. The CD99 and bcl-2 were selectively stained in the primitive NET, which was detected no later than a FA of 6 weeks. The CD34 and bcl-2 were positive in the immature-tooking precartilage blastornatous components, which proved useful for detecting immature cartilage, corresponding to a FA of 5 to 6 weeks. The ontogeny of IT was found to correspond to the embryonic stage at a FA of 2 to 8 weeks, and CD99, CD34, bcl-2, AFP, CD30, and PLAP could be used as supportive tools to define IT. This new grading system could be more scientific and more reproducible in any spectra of teratorna.

L22 ANSWER 9 OF 36 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
AN 2005:12993 BIOSIS
DN PREV200500018187
TI Bcl-2 homodimerization involves two distinct binding surfaces, a topographic arrangement that provides an effective mechanism for Bcl-2 to capture activated Bax.
AU Zhang, Zhi; Lapolla, Suzanne M.; Annis, Matthew G.; Truscott, Mary; Roberts, G. Jane; Miao, Yiwei; Shao, Yuanlong; Tan, Chibing; Peng, Jun; Johnson, Arthur E.; Zhang, Xuejun C.; Andrews, David W.; Lin, Jialing [Reprint Author]
CS Hlth Sci CtrDept Biochem and Mol Biol, Univ Oklahoma, 940 Stanton L Young Blvd,BMSB 935,POB 26901, Oklahoma City, OK, 73190, USA jialing-lin@ouhsc.edu
SO Journal of Biological Chemistry, (October 15 2004) Vol. 279, No. 42, pp. 43920-43928. print. CODEN: JBCHA3. ISSN: 0021-9258.
DT Article
LA English
ED Entered STN: 22 Dec 2004 Last Updated on STN: 22 Dec 2004
AB The homo- and heterodimerization of Bcl-2 family proteins is important for

transduction and integration of apoptotic signals and control of the permeability of mitochondria and endoplasmic reticulum membranes. Here we mapped the interface of the Bcl-2 homodimer in a cell-free system using site-specific photocross-linking. Bcl-2 homodimer-specific photoadducts were detected from 11 of 17 sites studied. When modeled into the structure of Bcl-2 core, the interface is composed of two distinct surfaces: an acceptor surface that includes the hydrophobic groove made by helices 2 and 8 and the loop connecting helices 4 and 5 and a donor surface that is made by helices 1-4 and the loop connecting helices 2 and 3. The two binding surfaces are on separate faces of the three-dimensional structure, explaining the formation of Bcl-2 homodimers, homo- oligomers, and Bcl-2/Bax hetero-oligomers. We show that in vitro the Bcl-2 dimer can still interact with activated Bax as a larger oligomer. However, formation of a Bax/Bcl-2 heterodimer is favored, since this interaction inhibits Bcl-2 homodimerization. Our data support a simple model mechanism by which Bcl-2 interacts with activated Bax during apoptosis in an effective manner to neutralize the proapoptotic activity of Bax.

L22 ANSWER 10 OF 36 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN

AN 2005:505777 BIOSIS

DN PREV200510301442

TI BCL-2 alpha in human telomerized corneal epithelial cells.

AU Robertson, D. M. [Reprint Author]; Cavanagh, H. D.; Shay, J. W.; Jester, J. V.

CS Univ Texas, SW Med Ctr, Dallas, TX 75230 USA

SO IOVS, (APR 2004) Vol. 45, No. Suppl. 1, pp. U562. Meeting Info.: Annual Meeting of the Association-for-Research-in-Vision-and-Ophthalmology. Ft Lauderdale, FL, USA. April 24 -29, 2004. Assoc Res Vis & Ophthalmol. CODEN: IOVSDA. ISSN: 0146-0404.

DT Conference; (Meeting)

Conference; (Meeting Poster)
LA English
ED Entered STN: 23 Nov 2005
Last Updated on STN: 23 Nov 2005
AB Purpose: In the human corneal epithelium, the proto-oncogene BCL-2
exhibits a gradient pattern of expression decreasing from limbus to
central cornea and basal to superficial layer, with a loss of expression
in surface epithelial cells prior to desquamation. The purpose of this
experiment is to examine the expression of BCL-2 in a normally
differentiating corneal epithelial cell line to validate this cell line as
a viable model for studying surface cell shedding in vitro. Methods:
Human Telomerized Corneal Epithelial (hTCEpi) cells immortalized with
human telomerase reverse transcriptase were grown on collagen
coatedculture inserts (Corning) submerged in KGM-2 culture medium
(Clonetics) containing 1.15 mM calcium for 7 days. Cells were then
air-lifted to induce differentiation and examined at day 0, 7 and 10.
Western Blotting using an anti-Keratin K3 antibody (Biogenesis) was used
to assess epithelial differentiation. Levels of Bcl-2 expression were
determined using an anti-BCL-2 monoclonal antibody (Ancell). RT PCR to
generate a 128 bp fragment crossing the intron/exon border of BCL-2 was
used to confirm the protein was splice variant alpha. Results:Consistent
with previously reported findings, following 7 days of air-lifted culture,
hTCEpi constructs differentiate in vitro similar to the human cornea in
vivo demonstrated by K3 expression. Western Blotting confirmed that the
26 kD BCL-2 protein is "pressed at all time points. Primers specific for
splice variant alpha confirmed that the 26 kD protein was BCL-
2 alpha. Conclusions: DISCUSSION: These data suggest
that hTCEpi cells express the full length BCL-2 transcript (splice variant
alpha) containing four conserved homology domains, aregulatory loop, and a
transmembrane domain; and that the BCL-2 protein is expressed in hTCEpi
cell constructs at all stages of differentiation. These findings

are in agreement with previously reported immunohistochemistry demonstrating BCL-2 in both the normal human cornea and our hTCEpi cell line. Taken together, these findings demonstrate a normal pattern of BCL-2 gene expression in the hTCEpi cell line, validating it as viable model for studying surface cell shedding in vitro.

L22 ANSWER 11 OF 36 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN DUPLICATE 2
AN 2003:555263 BIOSIS
DN PREV200300558218
TI Cycloheximide and actinomycin D delay death and affect bcl-2, bax, and Ice gene expression in astrocytes under in vitro ischemia.
AU Yu, Albert Cheung Hoi [Reprint Author]; Yung, Hon Wa; Hui, Michael Hung Kit; Lau, Lok Ting; Chen, Xiao Qian; Collins, Richard A.
CS Department of Neurobiology, Neuroscience Research Institute, Peking University, Peking University Health Science Center, 38 Xue Yuan Road, Beijing, 100083, China
achy@dnachip.com.hk; achy@bjmu.edu.cn
SO Journal of Neuroscience Research, (October 15 2003) Vol. 74, No. 2, pp. 318-325. print.
ISSN: 0360-4012 (ISSN print).
DT Article
LA English
ED Entered STN: 26 Nov 2003
Last Updated on STN: 26 Nov 2003
AB An in vitro ischemia model was established and the effect of the metabolic inhibitors cycloheximide (CHX) and actinomycin D (ActD) on apoptosis in astrocytes under ischemia studied. CHX decreased by 75% the number of cells dying after 6 hr of ischemia compared with control cultures. TdT-mediated dUTP nick end labelling (TUNEL) staining of comparable cultures was reduced by 40%. ActD decreased cell death by 60% compared with controls. The number of TUNEL-positive cells was reduced by 38%. The nuclear shrinkage in TUNEL-positive astrocytes in control cultures did not occur in ActD-treated astrocytes, indicating that nuclear shrinkage

and DNA fragmentation during apoptosis are two unrelated processes. Expression of bcl-2 (alpha and beta), bax, and Ice in astrocytes under similar ischemic conditions, as measured by quantitative reverse transcription-polymerase chain reaction, indicated that ischemia down-regulated bcl-2 (alpha and beta) and bax. Ice was initially down-regulated from 0 to 4 hr, before returning to control levels after 8 hr of ischemia. ActD decreased the expression of these genes. CHX reduced the expression of bcl-2 (alpha and beta) but increased bax and Ice expression. It is hypothesized that the balance of proapoptotic (Bad, Bax) and anti-apoptotic (Bcl-2, Bcl-XI) proteins determines apoptosis. The data suggest that the ratio of Bcl-2/Bad in astrocytes following ActD and CHX treatment does not decrease as much in untreated cells during ischemia. Our data indicate that it is the ratio of Bcl-2 family members that plays a critical role in determining ischemia-induced apoptosis. It is also important to note that ischemia-induced apoptosis involves the regulation of RNA and protein synthesis.

L22 ANSWER 12 OF 36 CAPLUS COPYRIGHT 2008 ACS on STN DUPLICATE 3
AN 2002:829670 CAPLUS
DN 138:85054
TI Bcl-2 and Porin Follow Different Pathways of TOM-dependent Insertion into the Mitochondrial Outer Membrane
AU Motz, Christian; Martin, Heiko; Krimmer, Thomas; Rassow, Joachim
CS Institut fur Mikrobiologie, Universitat Hohenheim, Stuttgart-Hohenheim, D-70593, Germany
SO Journal of Molecular Biology (2002), 323(4), 729-738
CODEN: JMOBAK; ISSN: 0022-2836
PB Elsevier Science Ltd.
DT Journal
LA English
AB The bcl-2 gene encodes a 26 kDa protein which functions as a central regulator of apoptosis. Here we investigated the pathway of Bcl -2α into the mitochondrial outer membrane using the yeast Saccharomyces cerevisiae as a model organism. We found that interactions of Bcl-2α with the mitochondrial import receptor Tom20 are dependent on two pos.

charged lysine residues in the immediate vicinity of the carboxy-terminal hydrophobic membrane anchor. The targeting function of these residues is independent of Tom22. Subsequent insertion of Bcl-2. alpha. into the mitochondrial outer membrane does not require Tom5 or Tom40, indicating that Bcl-2α bypasses the general import pore (GIP). Bcl-2. alpha. shows a unique pattern of interactions with the components of the mitochondrial TOM complex, demonstrating that at least two different pathways lead from the import receptor Tom20 into the mitochondrial outer membrane.
RE.CNT 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 13 OF 36 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
AN 2002:368762 BIOSIS
DN PREV200200368762
TI Dynamic membrane topology of Bcl-2 during apoptosis.
AU Kim, Peter K. [Reprint author]; Annis, Matthew G. [Reprint author]; Zhu, Weijia [Reprint author]; Falcone, Mina [Reprint author]; Leber, Brian; Andrews, David W. [Reprint author]
CS Biochemistry, McMaster University, 1200 Main St West, Hamilton, ON, L8NZ5, Canada
SO FASEB Journal, (March 20, 2002) Vol. 16, No. 4, pp. A522. print. Meeting Info.: Annual Meeting of the Professional Research Scientists on Experimental Biology. New Orleans, Louisiana, USA. April 20-24, 2002. CODEN: FAJOEC. ISSN: 0892-6638.
DT Conference; (Meeting) Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 3 Jul 2002 Last Updated on STN: 3 Jul 2002
AB Bcl-2 family proteins regulate apoptosis by multiple mechanisms including the formation of pores. The structure of Bcl-XL resembles that of diptheria toxin, a protein capable of forming pores in membranes. This observation initiated our study into the pore-forming capabilities of Bcl-2 in culture cells. The alpha5 and alpha6 helices of Bcl-2 are believed to insert into the membrane bilayer to form a pore. To assess the conformation of Bcl-2, we examined the local environment of

cys158, located in the alpha5 helix near the base of the pore forming region, and cys229, located in the transmembrane domain, using the lipid-impermeant cysteine modifying agent iodoacetylamino stilbene disulfonic acid (IASD). Only cys residues in the lipid bilayer are protected from modification by IASD. We demonstrate that cys158 of Bcl-2 is readily accessible in Rat 1 cells stably expressing wild type Bcl-2, the mitochondrial-specific mutant or the ER-specific mutant. However, upon induction of apoptosis cys158 is protected from modification (and hence integrated into membranes). This is the first in vivo evidence demonstrating the putative pore forming conformation of Bcl-2.

L22 ANSWER 14 OF 36 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2001:369365 CAPLUS
DN 135:316528
TI Protecting the myocardium from ischemic injury: A critical role for α1-Adrenoreceptors?
AU Salvi, Sundeep
CS Department of Medicine, Southampton General Hospital, Southampton, SO16 6YD, UK
SO Chest (2001), 119(4), 1242-1249
CODEN: CHETBF; ISSN: 0012-3692
PB American College of Chest Physicians
DT Journal; General Review
LA English
AB A review with 48 refs. Ischemic preconditioning (IPC) refers to the ability of short periods of ischemia to make the myocardium more resistant to a subsequent ischemic insult. It is the most powerful form of endogenous protection against myocardial infarction and was demonstrated in all species evaluated to date. However, the cellular mechanisms that drive IPC remain poorly understood. This hypothesis describes an important role for α1-adrenoreceptors in mediating IPC and discusses the underlying mechanisms by which this is likely achieved. α1-Adrenoreceptors are present in the myocardium of all mammalian species, and several lines of evidence suggest that they play an important role in mediating IPC. During periods of myocardial

hypoxia/ischemia, cardiomyocytes have to rely solely on anaerobic glycolysis for energy production; for this, the cells have to depend on increased glucose entry inside the cell as well as increased glycolysis. Stimulation of α1-adrenoreceptors increases glucose transport inside the cardiomyocytes by translocating glucose transporter (GLUT)-1 and GLUT-4 from the cytoplasm to the plasma membrane, enhances glycogenolysis by activating phosphorylase kinase, increases the rate of glycolysis by activating the enzyme phosphofructokinase, reduces intracellular acidity produced during excessive glycolysis by activating the Na+/H+ exchanger, and inhibits apoptosis by increasing the levels of the antiapoptotic protein Bcl-2. Myocardial ischemia produces an increase in the expression of α1-adrenoreceptors in cardiomyocytes, as well as increases the levels of its agonist norepinephrine by several fold. During ischemic states, upregulation of α1-adrenoreceptors and increase in norepinephrine release could be a powerful adaptive mechanism that drives IPC. An understanding into the role of α1-adrenoreceptors in mediating IPC could not only point to newer treatments for limiting myocardial damage during myocardial infarction or heart surgery, but could also help in avoiding the use of α1-antagonists in patients with ischemic heart disease.

RE.CNT 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 15 OF 36 EMBASE

AN 2002034170 EMBASE

TI BCL2 and BAX mRNA concentration profile in fibrillary astrocytoma.

AU Mazurek, U. (correspondence); Bierzynska-Macyszyn, G.; Gola, J.; Orchel, J.; Slowinski, J.; Wilczok, T.

CS Dept. Molec. Bio. Biochem/Biopharm., Medical University of Silesia, Narcyzow 1 Street, Sosnowiec, Poland. umazurek@farmant.slam.katowice.pl

SO Folia Histochemica et Cytobiologica, (2001) Vol. 39, No. SUPPL. 2, pp.

179-180.
Refs: 10
ISSN: 0239-8508 CODEN: FHCYEM
CY Poland
DT Journal; Conference Article; (Conference paper)
FS 014 Radiology
016 Cancer
029 Clinical and Experimental Biochemistry
030 Clinical and Experimental Pharmacology
037 Drug Literature Index
008 Neurology and Neurosurgery
LA English
SL English
ED Entered STN: 7 Feb 2002
Last Updated on STN: 7 Feb 2002
AB A high level of the BCL2 protein and the lack of apoptosis promoting protein BAX are beginning to be treated as markers of cellular resistance to anti-neoplastic drugs. The object of the study were specimens from stereotactic biopsy of astrocytoma fibrillare in the central brain area, inaccessible to conventional surgery. The cytological preparations have been evaluated with histopathological and immunohistochemical methods in order to determine the origin of the tumour and assess cell proliferation activity. The molecular analysis conducted in order to determine the sensitivity of the tumour to radio- or chemotherapy included the determination of the number of mRNA BCL2 alpha and beta molecules and of BAX in 1 μg total RNA obtained from microscope slides. A higher expression of BAX than of BCL2-alpha is a prognosis for a positive result of chemo- or radiotherapy. A trace number of mRNA BCL2-beta molecules and a smaller number of mRNA BCL2-alpha molecules than mRNA BAX is a good prognosis for therapy.

L22 ANSWER 16 OF 36 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN DUPLICATE 4
AN 2001:123816 BIOSIS
DN PREV200100123816
TI Effects of phenytoin on glutathione status and oxidative stress biomarker gene mRNA levels in cultured precision human liver slices.
AU Gallagher, Evan P. [Reprint author]; Sheehy, Karen M.
CS Department of Physiological Sciences and Center for Environmental and

Human Toxicology, University of Florida, Gainesville, FL, 32611-0885, USA
gallaghere@mail.vetmed.ufl.edu
SO Toxicological Sciences, (January, 2001) Vol. 59, No. 1, pp. 118-126.
print.
ISSN: 1096-6080.
DT Article
LA English
ED Entered STN: 7 Mar 2001
Last Updated on STN: 15 Feb 2002
AB Cellular production of reactive oxygen species (ROS) has been implicated as an important mechanism of chemical teratogenesis and developmental toxicity. Unfortunately, the lack of relevant model systems has precluded studies targeting the role of ROS in human teratogenesis and prenatal toxicity. In the current study, we have used cultured precision human prenatal liver slices to study the effects of the human teratogen phenytoin (diphenylhydantoin; Dilantin) on cell toxicity, glutathione redox status, and steady-state mRNA expression of a panel of oxidative stress-related biomarker genes. The biomarker genes analyzed were p53, bcl-2, alpha class glutathione S-transferases isozymes A1 and A4 (hGSTA1 and hGSTA4), and the catalytic subunit of gamma-glutamylcysteine synthetase (gammaGCS-HS). Liver slices (200 mum) were prepared from second trimester prenatal livers and cultured in the presence of 0, 250 muM, and 1000 muM phenytoin for 18 h. Exposure to 1000 muM phenytoin elicited 41% and 34% reductions in slice intracellular potassium and reduced glutathione (GSH) concentrations, respectively. The reduction in slice GSH concentrations at 1000 muM phenytoin was accompanied by a 2.2-fold increase in the percentage of total slice glutathione consisting of GSSG, and a 3.9-fold increase in hGSTA1 steady-state mRNA expression. Exposure to 250 muM or 1000 muM phenytoin also elicited a relatively minor (less than 2-fold) but significant increase in p53 steady-state mRNA expression. In contrast, the steady-state levels of gammaGCS-HS, hGSTA4, and bcl-2 mRNAs were not

affected by phenytoin exposure. Our findings in a relevant human model system are supportive of a protective role of GSH and hGSTA1 against phenytoin toxicity and teratogenesis. These studies also demonstrate the utility of using cultured human prenatal liver slices as a relevant tool for developmental toxicology studies.

L22 ANSWER 17 OF 36 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2000:380163 CAPLUS
DN 133:173639
TI Study of the Secondary Structure of the C-Terminal Domain of the Antiapoptotic Protein Bcl-2 and Its Interaction with Model Membranes
AU Martinez-Senac, Maria del Mar; Corbalan-Garcia, Senena; Gomez-Fernandez, Juan C.
CS Departamento de Bioquimica y Biologia Molecular A Facultad de Veterinaria, Universidad de Murcia, Murcia, E-30080, Spain
SO Biochemistry (2000), 39(26), 7744-7752
CODEN: BICHAW; ISSN: 0006-2960
PB American Chemical Society
DT Journal
LA English
AB Bcl-2 is a protein which inhibits programmed cell death. It is associated to many cell membranes such as mitochondrial outer membrane, endoplasmic reticulum, and nuclear envelope, apparently through a C-terminal hydrophobic domain. We have used IR spectroscopy to study the secondary structure of a synthetic peptide (a 23mer) with the same sequence as this C-terminal domain (residues 217-239) of Bcl-2. The spectrum of this peptide in D2O buffer shows an amide I' band with a maximum at 1622 cm-1, which clearly indicates its tendency to aggregate in aqueous solvent. However, the peptide incorporated in multilamellar phosphatidylcholine membranes shows a totally different spectrum of the amide I' band, with a maximum at 1655 cm-1, indicating a predominantly α-helical structure. Addition of the peptide to unilamellar vesicles destabilized them and released encapsulated carboxyfluorescein. Differential scanning calorimetry of dimyristoylphosphatidylcholine multilamellar vesicles in which the peptide

was incorporated revealed that increasing concns. of the peptide progressively broadened the pretransition and the main transition, as is to be expected for a membrane integral mol. Fluorescence polarization of 1,6-diphenyl-1,3,5-hexatriene in fluid phosphatidylcholine vesicles showed . that increasing concns. of the peptide produced increased polarization values, pointing to an increase in the apparent order of the membrane and indicating that high concns. of the peptide considerably broaden the phase transition of dimyristoylphosphatidylcholine multilamellar vesicles. Quenching the intrinsic fluorescence of the Tyr-235 of the peptide, by KI, indicated that this aminoacyl residue is highly exposed to aqueous solvent when incorporated in phospholipid vesicles. The results are discussed in terms of their relevance to the proposed topol. of insertion of Bcl-2 into biol. membranes.

RE.CNT 80 THERE ARE 80 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 18 OF 36 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN DUPLICATE 5

AN 2000:173007 BIOSIS
DN PREV200000173007
TI Gene expressions during the development and sexual differentiation of the olfactory bulb in rats.
AU Wong, C. C. [Reprint author]; Poon, W. H.; Tsim, T. Y.; Wong, Eugene Y. K.; Leung, M. S.
CS Department of Physiology, Chinese University of Hong Kong, Shatin, New Territories, Hongkong, China
SO Developmental Brain Research, (Feb. 7, 2000) Vol. 119, No. 2, pp. 187-194. print.
CODEN: DBRRDB. ISSN: 0165-3806.
DT Article
LA English
ED Entered STN: 3 May 2000
Last Updated on STN: 4 Jan 2002
AB In this study, expressions of cell-cycle-related genes: p53, retinoblastoma (Rb), p21, bcl-2alpha, bcl-2beta; protooncogene c-ski; glial cell marker protein gene S100beta; neurotransmitter gene, substance

P and sexual-differentiation-related genes, androgen receptor (AR) and estrogen receptor beta (ERbeta), are studied in the olfactory bulb of groups of both six female and six male rats at the ages of 3, 10, 20 and 40 days. Expressions of housekeeping genes such as beta-actin, cyclophilin and proliferating cell nuclear antigens (PCNA) are determined using reverse transcription polymerase chain reaction (RT-PCR) for the correction of unequal amount of cDNA added into the samples. Using labeled 32P-dCTP and Phosphorimager technology, relative abundance of radioactivities of the PCR products is obtained by dividing the radioactivity of each individual sample by the corresponding radioactivities of different housekeeping genes. Data evaluated by Two-way ANOVA indicate that only the bcl-2alpha gene expression is affected significantly by age, sex and their interactions no matter which of the three housekeeping genes is used for correction. When beta-actin was used for corrections, effects of age but not sex were found in the expressions of p53, Rb, p21, AR, ERbeta, substance P and S100beta genes, but not in bcl-2beta, c-ski, cyclophilin and PCNA genes. While cyclophilin was used for corrections, only the p53, Rb, AR, ERbeta, substance P and S100beta but not the bcl-2beta, p21, c-ski, PCNA and beta-actin genes are affected by age. They are all not influenced by sex of the animals. Only the AR, ERbeta and S100beta genes are age-dependent when PCNA was used for the correction. The other gene expressions are not altered by sex, while the interactions of age and sex were found to be significantly affecting the bcl-2beta gene expression. Conclusively, developmental changes of the p53, Rb, AR, ERbeta, substance P and S100beta genes expressions are quite evidenced while only the bcl-2alpha gene seems to change significantly during the sexual differentiation of olfactory bulb in rats.

L22 ANSWER 19 OF 36 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN

AN 2001:71196 BIOSIS
DN PREV200100071196
TI Genes expression in the sorted Merkel cells in sinus hair follicles of the rat.
AU Leung, M. S. [Reprint author]; Poon, W. H.; Wong, C. C.
CS Chinese Univ Hong Kong, Shatin NT, Hong Kong
SO Society for Neuroscience Abstracts, (2000) Vol. 26, No. 1-2, pp. Abstract No.-155.4. print.
Meeting Info.: 30th Annual Meeting of the Society of Neuroscience. New Orleans, LA, USA. November 04-09, 2000. Society for Neuroscience.
ISSN: 0190-5295.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 7 Feb 2001
Last Updated on STN: 12 Feb 2002
AB Merkel cell-neurite complexes are the slowly adapting type II cutaneous mechanoreceptors. They consisted of a cluster of Merkel cells with attachment of adjacent nerve terminals which respond to light touch on the skin. Vibrissal hair on the face of male rats (apprx 200 gm) was excised out for the dissection of the ring of Merkel cells from the sinus hair follicle. The samples were loaded with quinarcrine and digested with Dispase to dissociate the cutaneous cells. The fluorescence labeled Merkel cells and controls (no flourescnece) were sorted out with a Coulter Epic Altra flow cytometer into tubes with lysing buffer for subsequent RNA extraction. The total RNA extracted were subjected to reverse transcription to get the cDNA. PCR were then carried out using 32P-labeled dCTP and specific primers for the different genes for programmed cell death and cellular signalling. In order to semi-quantitate the relative amount of mRNA for the different neuropeptides found in the Merkel cells, the amount of mRNA for the household gene beta-actin was employed to normalized the results for different target genes. The radioactive labeled PCR products after 8% native polyacrylamide gel electrophoresis were quantified using a phosphorimager. Programmed cell death related genes like caspace-1, caspace3, bcl-x, BAX, BAD, CSR and calcineurin A were expressed in Merkel

and adjacent cutaneous cells; bcl-2alpha, bcl-2beta, NGFI-A and NGFI-B
were detected in Merkel cells only. Interesstingly NGFI-C was expressed
in the control cells only. For the cellular signalling related genes,
unlike most of the genes studied, ryanodine receptor type 2 genes was
expressed in control cells only.

L22 ANSWER 20 OF 36 CAPLUS COPYRIGHT 2008 ACS on STN
AN 1999:135058 CAPLUS
DN 130:295067
TI Nuclear localization of β-catenin and loss of apical brush border
actin in cystic tubules of bcl-2 -/- mice
AU Sorenson, Christine M.
CS George M. O'Brien Kidney and Urological Diseases Center, Renal Division,
Department of Medicine, Washington University School of Medicine, St.
Louis, MO, 63110, USA
SO American Journal of Physiology (1999), 276(2, Pt. 2), F210-F217
CODEN: AJPHAP; ISSN: 0002-9513
PB American Physiological Society
DT Journal
LA English
AB Tight regulation of the rates of cell proliferation and apoptosis is critical
for normal nephrogenesis. Nephrogenesis is profoundly affected by the
loss of bcl-2 expression. Bcl-2-deficient (bcl-2 -/-) mice are
born with renal hypoplasia and succumb to renal failure secondary to renal
multicystic disease. Cell-cell and cell-matrix interactions impact tissue
architecture by modulating cell proliferation, migration, differentiation,
and apoptosis. E-cadherin mediates calcium-dependent homotypic cell-cell
interactions that are stabilized by its association with catenins
and the actin cytoskeleton. The contribution of altered cell-cell
interactions to renal cystic disease has not been delineated. Cystic
kidneys from bcl-2 -/- mice displayed nuclear localization of
β-catenin and loss of apical brush border actin staining. The
protein levels of α-catenin, β-catenin, actin, and E-cadherin
were not altered in cystic kidneys compared with normal kidneys.
Therefore, an altered distribution of β-catenin and actin, in kidneys
from bcl-2 -/- mice, may indicate improper cell-cell interactions

interfering with renal maturation and contributing to renal cyst formation.
RE.CNT 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 21 OF 36 CAPLUS COPYRIGHT 2008 ACS on STN DUPLICATE 6
AN 1998:763358 CAPLUS
DN 130:91864
TI Cytoprotection by Bcl-2 requires the pore-forming α5 and α6 helixes
AU Matsuyama, Shigemi; Schendel, Sharon L.; Xie, Zhihua; Reed, John C.
CS Burnham Institute, Program on Apoptosis and Cell Death Research, La Jolla,
CA, 92037, USA
SO Journal of Biological Chemistry (1998), 273(47), 30995-31001
CODEN: JBCHA3; ISSN: 0021-9258
PB American Society for Biochemistry and Molecular Biology
DT Journal
LA English
AB We explored whether the putative channel-forming fifth and sixth α-helixes of Bcl-2 and Bax account for Bcl-2-mediated cell survival
and Bax-induced cell death in mammalian cells and in the yeast Saccharomyces cerevisiae. When α5-α6 were either deleted or swapped with each other, the Bcl-2Δα5α6 deletion mutant and Bcl-2-Bax(α5α6) chimeric protein failed to block apoptosis induced by either Bax or staurosporine in human cells and were unable to
prevent Bax-induced cell death in yeast, implying that the α5-α6 region of Bcl-2 is essential for its cytoprotective function. Addnl. expts. indicated that, although α5-α6 is necessary, it is also insufficient for the anti-apoptotic activity of
Bcl-2. In contrast, deletion or substitution of α5-α6 in Bax reduced but did not abrogate apoptosis induction in human cells, whereas
it did completely nullify cytotoxic activity in yeast, implying that the
pore-forming segments of Bax are critical for conferring a lethal phenotype in yeast but not necessarily in human cells. BaxΔα5α6 and Bax- Bcl-2(.
alpha.5α6) also retained the ability to dimerize with Bcl-2. Bax therefore may have redundant mechanisms for inducing apoptosis in
mammalian cells, based on its ability to form α5-α6-dependent channels in membranes and to dimerize with and antagonize anti-apoptotic
proteins such as Bcl-2.
RE.CNT 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 22 OF 36 CAPLUS COPYRIGHT 2008 ACS on STN DUPLICATE 7
AN 1998:54978 CAPLUS
DN 128:178931
OREF 128:35275a,35278a
TI Alteration of proteins regulating apoptosis, Bcl-2, Bcl-x, Bax, Bak, Bad,
ICH-1 and CPP32, in Alzheimer's disease
AU Kitamura, Yoshihisa; Shimohama, Shun; Kamoshima, Wataru; Ota, Takashi;
Matsuoka, Yasuji; Nomura, Yasuyuki; Smith, Mark A.; Perry, George;
Whitehouse, Peter J.; Taniguchi, Takashi
CS Department of Neurobiology, Kyoto Pharmaceutical University, Kyoto, Japan
SO Brain Research (1998), 780(2), 260-269
CODEN: BRREAP; ISSN: 0006-8993
PB Elsevier Science B.V.
DT Journal
LA English
AB Recently, apoptosis has been implicated in the selective neuronal loss of
Alzheimer's disease (AD). Apoptosis is regulated by the B cell leukemia-2
gene product (Bcl-2) family (Bcl-2, Bcl-x, Bax, Bak and Bad) and the
caspase family (ICH-1 and CPP32), with apoptosis being prevented by Bcl-2
and Bcl-x, and promoted by Bax, Bak, Bad, ICH-1 and CPP32. In the present
study, we examined the levels of these proteins in the membranous and
cytosolic fractions of temporal cortex in AD and control brain. In the
membranous fraction, the levels of Bcl-2.alpha
., Bcl-xL, Bcl-xβ, Bak and Bad were increased in AD. In the
cytosolic fractions, the level of Bcl-xβ was increased, while Bcl-xL,
Bax, Bak, Bad and ICH-1L were unchanged. CPP32 was not detected in AD or
control brain. These findings demonstrate a differential involvement of
cell death-regulatory proteins in AD and suggest that Bak, Bad, Bcl-2 and
Bcl-x are upregulated in AD brains.
RE.CNT 68 THERE ARE 68 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 23 OF 36 CAPLUS COPYRIGHT 2008 ACS on STN
AN 1997:346522 CAPLUS
DN 127:93998
OREF 127:18073a,18076a
TI Analysis of a sequenced cDNA library from multiple sclerosis lesions

AU Becker, Kevin G.; Mattson, David H.; Powers, James M.; Gado, Ameer M.;
Biddison, William E.
CS Molecular Immunology Section, Neuroimmunology Branch, National Institute
of Neurological Disorders and Stroke, National Institutes of Health,
Bethesda MD, USA
SO Journal of Neuroimmunology (1997), 77(1), 27-38
CODEN: JNRIDW; ISSN: 0165-5728
PB Elsevier
DT Journal
LA English
AB To identify genes that are expressed in MS pathogenesis, the
authors have analyzed a normalized cDNA library made from mRNA obtained
from CNS lesions of a patient with primary progressive MS. Complementary
DNA clones obtained from this library were subjected to automated DNA
sequencing to generate expressed sequence tags. Anal. of this MS cDNA
library revealed the presence of 54 cDNAs that were associated with immune
activation and indicated the presence of an ongoing inflammatory response
with evidence of both cell-mediated and humoral immune responses. The
surprising finding was that 16 of the cDNAs encoded autoantigens associated
with seven other autoimmune disorders, while only three of these 16
autoantigen cDNAs were present in a similarly constructed adult brain
library. Such aberrant autoantigen expression could provide a source of
secondary autoimmune stimulation that could contribute to the ongoing
inflammatory response in MS. In addition, two cDNAs were found that mapped
to a known MS susceptibility locus (5p14-p12): one encoded an excitatory
amino acid transporter and the other a human homolog of the Drosophila
disabled gene. This approach to the mol. biol. of MS pathogenesis may
help to illuminate previously unappreciated aspects of this disease.

AN 1996274872 EMBASE
TI [The expanding Bcl2 gene family: Towards a comprehensive approach of the
structure/activity relationship of proteins].
L'expansion continue de la famille Bcl2. Vers une approche raisonnee des
relations structure/activite?.
AU Larsen, C.-J. (correspondence)
CS INSERM U 301, Institut de Genetique Moleculaire, 27, Rue Juliette-Dodu,
75010 Paris, France.
SO Hematologie, (1996) Vol. 2, No. 4, pp. 301-311.
ISSN: 1264-7527 CODEN: HEMAF2
CY France
DT Journal; General Review; (Review)
FS 016 Cancer
022 Human Genetics
025 Hematology
LA French
SL French; English
ED Entered STN: 15 Oct 1996
Last Updated on STN: 15 Oct 1996
AB bcl2 gene is the most representative member of a growing family of genes
which counts among the main regulators of programmed cell death or
apoptosis. Some of the protein members of the family (bcl-2α , bcl-x(L)) inhibit the cell death process
(subfamily 1), whereas others (bax, bak, bik) promote apoptosis (subfamily
2). These functions appear to be carried out through heterodimerization,
between members of each subfamily. Numerous works have shown that two
highly conserved domains (BH1 and BH2) are needed for
heterodimerization and for biological activity. In this review, recent
data are presented on the presence of other conserved domains
(BH3, NH1, NH2) that appear to be necessary for heterodimerization between
members of the BCL2 family as well as for interactions with other cellular
proteins. The implication of these new features in the physiopathology of
programmed cell death in hematopoiesis and hematopoietical malignancies,
is discussed.

L22 ANSWER 25 OF 36 CAPLUS COPYRIGHT 2008 ACS on STN
AN 1995:652012 CAPLUS
DN 123:80240
OREF 123:14247a,14250a

TI The α5β1 integrin supports survival of cells on fibronectin and up-regulates Bcl-2 expression
AU Zhang, Zhuohua; Vuori, Kristiina; Reed, John C.; Ruoslahti, Erkki
CS Cancer Res. Cent., La Jolla Cancer Res. Foundation, La Jolla, CA, 92037, USA
SO Proceedings of the National Academy of Sciences of the United States of America (1995), 92(13), 6161-5
CODEN: PNASA6; ISSN: 0027-8424
PB National Academy of Sciences
DT Journal
LA English
AB Anchorage-dependent cells that are prevented from attaching to an extracellular matrix substrate stop proliferating and may undergo apoptosis. Cell adhesion to a substrate is mediated by the integrin family of cell surface receptors, which are known to elicit intracellular signals upon cell adhesion. We show here that Chinese hamster ovary cells expressing the α5β1 integrin, which is a fibronectin receptor, do not undergo apoptosis upon serum withdrawal when the cells are plated on fibronectin. However, the αvβ1 integrin, which is also a fibronectin receptor and binds fibronectin on the same RGD motif as α5β1, did not prevent apoptosis on fibronectin of the same cells. The cytoplasmic domain of the integrin α5 subunit was required for the α5β1-mediated cell survival on fibronectin. The fibronectin-mediated survival effect appeared to be independent of the level of tyrosine phosphorylation of the focal adhesion kinase, which is induced by integrin-mediated cell attachment. The expression of the Bcl-2 protein, which counteracts apoptosis, was elevated in cells attaching to fibronectin through α5β1; cells attaching through αvβ1 survived only if exogenous Bcl-2 was provided. Thus, α5β1, but not the closely related αvβ1 integrin, appears to suppress apoptotic cell death through the Bcl-2 pathway.

L22 ANSWER 26 OF 36 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN DUPLICATE 8
AN 1994:299652 BIOSIS
DN PREV199497312652
TI Targeted disruption of Bcl-2-alpha-beta in mice: Occurrence of gray hair, polycystic disease, and lymphocytopenia.
AU Nakayama, Keiko; Nakayama, Kei-Ichi; Negishi, Izumi; Kuida, Keisuke; Sawa,

Hirofumi; Loh, Dennis Y.
CS Howard Hughes Med. Inst., Dep. Med. Genetics, Washington University Sch.
Med., St. Louis, MO 63110, USA
SO Proceedings of the National Academy of Sciences of the United States of
America, (1994) Vol. 91, No. 9, pp. 3700-3704.
CODEN: PNASA6. ISSN: 0027-8424.
DT Article
LA English
ED Entered STN: 13 Jul 1994
Last Updated on STN: 14 Jul 1994
AB Mice carrying ablated coding regions of the bcl-2-
alpha and bcl-2-beta transcripts have been made. bcl-2-/- mutants
are smaller but viable, although about half of them die by 6 weeks
of age. As shown earlier with somatic bcl-2 gene-targeted mice, the
number of lymphocytes markedly decreased within few weeks after birth
while other hematopoietic lineages remained unaffected. Among
lymphocytes, CD8+ T cells disappeared most quickly followed by CD4+ T
cells, whereas B cells were least affected. bcl-2-/- lymphocytes, however,
could respond normally to various stimuli including anti-CD3, Con A,
phorbol 12-myristate 13-acetate plus ionomycin, interleukin 2,
lipopolysaccharide, and anti-IgM antibody. Abnormalities among
nonlymphoid organs include smaller auricles, hair color turning gray at
4-5 weeks of age, and polycystic kidney disease-like change of renal
tubules. These results suggest that Bcl-2 may be involved during
morphogenesis where inductive interactions between epithelium and
mesenchyme are important such as in the kidneys, hair follicles,
and perichondrium of auricles. Surprisingly, the nervous system,
intestines, and skin appear normal despite the fact that these organs show
high levels of endogeneous Bcl-2 expression in normal mice.

L22 ANSWER 27 OF 36 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on
STN DUPLICATE 9
AN 1994:446674 BIOSIS
DN PREV199497459674
TI The protein bcl-2-alpha does not require
membrane attachment, but two conserved domains to suppress apoptosis.
AU Borner, Christoph; Martinou, Isabelle; Mattmann, Chantal; Irmler, Martin;
Schaerer, Esther; Martinou, Jean-Claude; Tschopp, Juerg [Reprint author]

CS Inst. Biochem., Chemin des Boveresses 155, CH-1066 Epalinges, Switzerland
SO Journal of Cell Biology, (1994) Vol. 126, No. 4, pp. 1059-1068.
CODEN: JCLBA3. ISSN: 0021-9525.
DT Article
LA English
ED Entered STN: 24 Oct 1994
Last Updated on STN: 24 Oct 1994
AB Bcl-2 is a mitochondrial- and perinuclear-associated protein that prolongs the lifespan of a variety of cell types by interfering with programmed cell death (apoptosis). Bcl-2 seems to function in an antioxidant pathway, and it is believed that membrane attachment mediated by a COOH-terminal hydrophobic tail is required for its full activity. To identify critical regions in bcl-2-alpha for subcellular localization, activity, and/or interaction with other proteins, we created, by site-directed mutagenesis, various deletion, truncation, and point mutations. We show here that membrane attachment is not required for the survival activity of bcl-2-alpha. A truncation mutant of bcl-2-alpha lacking the last 33 amino acids (T3.1) including the hydrophobic COOH terminus shows full activity in blocking apoptosis of nerve growth factor-deprived sympathetic neurons or TNF-alpha-treated L929 fibroblasts. Confocal microscopy reveals that the T3 mutant departs into the extremities of neurites in neurons and filopodias in fibroblasts. Consistently, T3 is predominantly detected in the soluble fraction by Western blotting, and is not inserted into microsomes after in vitro transcription/translation. We further provide evidence for motifs (S-N and S-II) at the NH-2 and COOH terminus of bcl-2, which are crucial for its activity.

L22 ANSWER 28 OF 36 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN DUPLICATE 10
AN 1995:342154 BIOSIS
DN PREV199598356454
TI Dissection of functional domains in Bcl-2-alpha by site-directed mutagenesis.
AU Borner, Christoph [Reprint author]; Olivier, Reynald; Martinou, Isabelle;

Martinou, Jean-Claude
CS Inst. Biochem., Univ. Fribourg, Rue du Musee 5, Perolles, CH-1700 Fribourg, Switzerland
SO Biochemistry and Cell Biology, (1994) Vol. 72, No. 11-12, pp. 463-469.
CODEN: BCBIEQ. ISSN: 0829-8211.
DT Article
LA English
ED Entered STN: 10 Aug 1995
Last Updated on STN: 10 Aug 1995
AB Bcl-2-alpha is a mitochondrial or perinuclear-associated oncoprotein that prolongs the life span of a variety of cell types by interfering with programmed cell death. How Bcl-2 confers cell survival is unknown, although antioxidant and antiprotease functions have been proposed. In addition, protein structures of Bcl-2 that are crucial for its survival activity are still ill-defined. Bcl-2 can occur as Bcl-2 -alpha or Bcl-2-beta, two alternatively spliced forms which solely differ in their carboxyl termini. The finding that Bcl-2-alpha is active and membrane bound, but Bcl-2-beta is inactive and cytosolic, indicates that the carboxyl terminus contributes to the survival activity of Bcl-2. This region contains two subdomains, a domain X with unknown function and a hydrophobic stretch reported to mediate membrane association of Bcl-2-alpha.
Recently Bcl-2-related proteins have been identified. These include Bax that heterodimerizes with Bcl-2 and, when overxpressed, counteracts Bcl-2.
Bax contains two highly conserved regions of sequence homology with Bcl-2, referred to as Bcl-2 homology 1 and 2 (BH1 and BH2) domains. Site-directed mutagenesis studies have revealed that both domains are not only novel dimerization motifs for the interaction of Bax with Bcl-2 but also crucial for the survival activity of Bcl-2. Interestingly, the C-terminal end of BH2 encompasses the Bcl-2-alpha/beta splice site, as well as part of domain X in Bcl-2-alpha. To better define the role of domain X and the hydrophobic C-terminal stretch of Bcl-2 -alpha for its survival activity, we created various deletion and truncation mutations in these regions by site-directed mutagenesis.
We show here that membrane attachment and therefore the hydrophobic stretch is not required for the survival activity of Bcl-2, but part of domain X appears to be indispensable.

L22 ANSWER 29 OF 36 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on
STN DUPLICATE 11
AN 1995:124497 BIOSIS
DN PREV199598138797
TI The BCL2 gene is the prototype of a gene family that controls programmed
cell death (apoptosis).
AU Larsen, C.-J
CS INSERM U-301 SDI 159541 CNRS, Inst. Genetique Moleculaire, 27 rue J. Dodu,
75010 Paris, France
SO Annales de Genetique, (1994) Vol. 37, No. 3, pp. 121-134.
CODEN: AGTQAH. ISSN: 0003-3995.
DT Article
General Review; (Literature Review)
LA French
ED Entered STN: 29 Mar 1995
Last Updated on STN: 29 Mar 1995
AB The BCL2 gene is the most representative member of a family of genes that
control cell homeostatic processes in the course of the developmental and
adult life. Some members of the BCL2 family (bcl-2-
alpha, bcl-x-L) inhibit apoptosis, whereas some others (Bax,
Bclx-s) induce it. The biological activity of these proteins is dictated
by: 1) their capacity to be integrated in specific membranes of the
cytoplasm; 2) their ability to homo- or heterodimerize, due to the
presence of two highly conserved domains which are a signature
of this gene family. The bcl-2 protein exhibits two main biochemical
properties: it acts in an antioxidant metabolic pathway aimed at
eliminating oxygen free radicals that induce lesions in DNA, lipids and
proteins; it modulates intracellular Ca++ fluxes. BCL2 (and presumably
its congeners) interplay with other genes involved in the tight control of
cell proliferation and programmed cell death (c-myc, p53). A more
comprehensive view of BCL2 functions should benefit to cancer chemotherapy
by improving rational approach of the antitumor drug mechanisms.

L22 ANSWER 30 OF 36 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on
STN DUPLICATE 12
AN 1994:127756 BIOSIS
DN PREV199497140756

TI Developmental regulation of bcl-2 expression in the thymus.
AU Moore, N. C. [Reprint author]; Anderson, G.; Williams, G. T.; Owen, J. J.
T.; Jenkinson, E. J.
CS Centre Clinical Res. Immunology Signalling, Med. Sch., Univ. Birmingham,
Birmingham B15 2TT, UK
SO Immunology, (1994) Vol. 81, No. 1, pp. 115-119.
CODEN: IMMUAM. ISSN: 0019-2805.
DT Article
LA English
ED Entered STN: 24 Mar 1994
Last Updated on STN: 24 Mar 1994
AB An important factor in shaping the T-cell receptor (TcR) repertoire during
thymocyte development is the susceptibility of double-positive (CD4+ CD8+)
thymocytes to induction of apoptosis (negative selection) when the TcR is
engaged by 'self'-antigens. Recent evidence has suggested that this
susceptibility to apoptosis may be influenced by the expression of bcl-2,
a proto-oncogene known to increase the resistance to apoptosis in various
cell systems. Using a semi-quantitative polymerase chain reaction (PCR)
technique in conjunction with staged embryonic material and purified
thymocyte subpopulations we have investigated patterns of bcl-2 expression
during normal T-cell development. Our results show that while bcl
-2-alpha gene expression is readily detectable in
immature CD3- CD4- CD8- thymocytes and in mature single-positive TcR-hi
cells, it is drastically reduced in TcR negative double-positive (CD3-
CD4+ CD8+) cortical thymocytes of intermediate maturity. Careful mapping
of bcl-2-alpha re-expression in relation to
the onset of TcR expression within the population of embryonic thymocytes
indicates that bcl-2-alpha is up-regulated
as soon as TcR molecules are expressed on the surface of CD4+
CD8+ thymocytes. Therefore, thymocytes susceptible to apoptosis on TcR
ligation express bcl-2-alpha mRNA suggesting
that changing levels of bcl-2 expression are unlikely to be the
only determinant regulating susceptibility to apoptosis in the thymus.
The possible implications of these changes in bcl-2 expression regarding

other facets of thymocyte development will be discussed.

L22 ANSWER 31 OF 36 CAPLUS COPYRIGHT 2008 ACS on STN
AN 1990:402214 CAPLUS
DN 113:2214
OREF 113:447a,450a
TI Charge configurations in oncogene products and transforming proteins
AU Karlin, Samuel; Brendel, Volker
CS Dep. Math., Stanford Univ., Stanford, CA, 94305, USA
SO Oncogene (1990), 5(1), 85-95
CODEN: ONCNES; ISSN: 0950-9232
DT Journal
LA English
AB Statistically significant charge clusters are of infrequent occurrence in all kinds of proteins. In the 6 standard classes of protooncogene products, all of the nuclear class contain a significant charge cluster and several, but not all, of the transmembrane class do, whereas significant charge clusters or patterns are not found in protooncogenes of primarily cytoplasmic location, nor in membrane-bound (src-like) protooncogenes, nor in those of the ras family. Among nuclear oncogene families, such as myc-, jun-, fos-, myb-, or ets-related, and among homologous proteins across species, the significant charge clusters are part of the most conserved region. These gene families generally have similar charge distributions embodying a significant charge cluster, not of an invariant sign, preceded by a substantial uncharged stretch of predominantly polar residues. Nuclear transforming proteins p53 and p68 also contain significant charge clusters together with long uncharged segments, suggestive of a modular structure of these proteins. Transmembrane oncogene c-mas contains a mixed charge cluster and c-fms displays an unusual (0, +)7 pattern, in both cases positioned within their intracellular activating domain. Distinctive charge configurations for excreted protooncogenes are of a mixed character. Possible functions, mechanisms, and associated exptl. procedures for studying proteins with anomalous charge distributions are discussed.

L22 ANSWER 32 OF 36 EMBASE COPYRIGHT (c) 2008 Elsevier B.V. All rights
reserved on STN
AN 1989273433 EMBASE
TI Stress-resistance conferred by high level of bcl-2.
alpha. protein in human B lymphoblastoid cell.
AU Tsujimoto, Y.
CS The Wistar Institute of Anatomy and Biology, Philadelphia, PA 19104,
United States.
SO Oncogene, (1989) Vol. 4, No. 11, pp. 1331-1336.
ISSN: 0950-9232 CODEN: ONCNES
CY United Kingdom
DT Journal; Article
FS 025 Hematology
029 Clinical and Experimental Biochemistry
LA English
SL English
ED Entered STN: 12 Dec 1991
Last Updated on STN: 12 Dec 1991
AB High levels of human bcl-2 protein(s) result in (i) the tumorgenic
conversion of mouse NIH3T3 cells, (ii) the better survival of mouse
myeloid cells in the absence of the required growth factor and (iii) give
a growth advantage to human EBV-lymphoblastoid B cells both in low serum
medium and limiting dilutions. The effect of the high levels of bcl-2
protein in EBV-B cells was further investigated. This revealed that high
levels of bcl-2α protein made EBV-B
cells more resistant to a variety of stresses including the application of
heat shock, ethanol, methotrexate and the absence of serum. Stress
resistance was not observed in EBV-B cells with elevated level of c-myc
protein. The mechanism of stress resistance conferred by the bcl
-2α protein is yet to be determined although the
resistance does not seem to be the result of an increase in major heat
shock proteins, hsp70 and hsp90, nor the arrest of cells in G(1)/G(0)
phase. The increased viability was observed in control transfectants but
not in bcl-2 transfectants when cells are seeded at higher
density in the absence of serum. Thus the improved survival of cells as a
result of high levels of the bcl-2α
protein is not specific to the absence of growth factor but is found to

occur with a variety of stresses.

L22 ANSWER 33 OF 36 CAPLUS COPYRIGHT 2008 ACS on STN
AN 1988:566863 CAPLUS
DN 109:166863
OREF 109:27599a,27602a
TI Diagnostic methods for detecting human lymphomas associated with chromosome 14 and 18 translocations and cloning, expression, and nucleotide sequence of human bcl-2 gene
IN Tsujimoto, Yoshihide; Croce, Carlos M.
PA Wistar Corp., USA
SO Eur. Pat. Appl., 23 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 252685	A2	19880113	EP 1987-305863	19870702
	EP 252685	A3	19900711		
	EP 252685	B1	19930616		
	R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
	US 5015568	A	19910514	US 1986-883687	19860709
	AT 90792	T	19930715	AT 1987-305863	19870702
	ES 2003064	T3	19940901	ES 1987-305863	19870702
	AU 8775328	A	19880218	AU 1987-75328	19870708
	AU 602704	B2	19901025		
	CA 1340827	C	19991123	CA 1987-541606	19870708
	JP 63100379	A	19880502	JP 1987-172023	19870709
	US 5202429	A	19930413	US 1991-663010	19910319
	US 5595869	A	19970121	US 1992-994941	19921223
	US 5459251	A	19951017	US 1994-228704	19940418
	US 5506344	A	19960409	US 1995-435193	19950505
	US 5523393	A	19960604	US 1995-435181	19950505
PRAI	US 1986-883687	A	19860709		
	EP 1987-305863	A	19870702		
	US 1991-633010	A1	19910319		
	US 1991-663010	A1	19910319		

US 1992-994941 A1 19921223
US 1994-228704 A3 19940418

AB Assays are provided for detecting a class of B-cell neoplasms associated with a chromosome translocation between chromosomes 14 and 18 which is involved in a majority of human follicular lymphomas. One assay uses an antibody immunoreactive with a protein overexpressed due to the chromosome translocation. Another assay involves measurement of the amount of mRNA which hybridizes to the gene proximal to the translocation breakpoint. The sequences of the protein-encoding regions of the bcl-2 gene are provided as well as bacterial clones which produce the proteins. A cDNA library from poly(A)+ mRNA of the pre-B-cell leukemia line 380 was constructed and cloned into λgt11 phage vectors, and recombinant clones were screened with a DNA probe consisting of a segment of chromosome 18 which spans the hotspot of breakpoints of the translocation of chromosome 18 to chromosome 14. Three independent but overlapping cDNA clones were obtained. The nucleotide sequences of both strands of the 5.5- and 3.5-kilobase transcripts were determined The DNA sequence of 5105 base pairs of the former reveals one possible open reading frame of 239 amino acid residues (bcl-2-. alpha.). The latter transcript codes for a 205-amino-acid residue protein (bcl-2β), differing from bcl-2. alpha. protein at the C-terminus.

L22 ANSWER 34 OF 36 EMBASE

AN 1988264412 EMBASE
TI Oncogenic potential of bcl-2 demonstrated by gene transfer.
AU Reed, J.C.; Cuddy, M.; Slabiak, T.; Croce, C.M.; Nowell, P.C.
CS Department of Pathology and Laboratory Medicine, University of Pennsylvania School of Medicine, Philadelphia, PA 19104-6082, United States.
SO Nature, (1988) Vol. 336, No. 6196, pp. 259-261.
ISSN: 0028-0836 CODEN: NATUAS
CY United Kingdom
DT Journal; Article
FS 016 Cancer

LA English
SL English
ED Entered STN: 11 Dec 1991
Last Updated on STN: 11 Dec 1991
AB Follicular lymphoma is the most common human B-cell malignancy in the
United States and Western Europe. Most of the tumours contain t(14;18)
chromosome translocations involving the human bcl-2 gene. Translocation
of bcl-2 sequences from chromosome 18 into the transcriptionally active
immunoglobulin locus at chromosome band 14q32 in B cells deregulates bcl-2
gene expression, resulting in the accumulation of high levels of bcl-2
messenger. Human bcl-2 transcripts generate two proteins, p26 bcl
-2-α and p22 bcl-2-β, by virtue of
alternative splice-site selection. Both proteins have in common their
first 196 NH(2)-terminal aminoacids but share little similarity with other
sequences in a data bank. Although the biological and biochemical
functions of bcl-2 are unknown, recent subcellular localization
studies indicate that p26 bcl-2-α
associates with cellular membranes, consistent with a stretch of
hydrophobic amino acids in its carboxy terminus. The blc-2 gene may
represent a novel oncogene having no known retroviral counterpart. Here
we demonstrate the oncogenic potential of bcl-2 through a gene transfer
approach.

L22 ANSWER 35 OF 36 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on
STN DUPLICATE 13
AN 1986:437567 BIOSIS
DN PREV198682103755; BA82:103755
TI ANALYSIS OF THE STRUCTURE TRANSCRIPTS AND PROTEIN PRODUCTS OF BCL-2 THE
GENE INVOLVED IN HUMAN FOLLICULAR LYMPHOMA.
AU TSUJIMOTO Y [Reprint author]; CROCE C M
CS WISTAR INST, 3601 SPRUCE ST, PHILADELPHIA, PA 19104, USA
SO Proceedings of the National Academy of Sciences of the United States of
America, (1986) Vol. 83, No. 14, pp. 5214-5218.
CODEN: PNASA6. ISSN: 0027-8424.
DT Article
FS BA

LA ENGLISH
ED Entered STN: 8 Nov 1986
Last Updated on STN: 8 Nov 1986
AB We have determined that the bcl-2 (B-cell leukemia/lymphoma 2) gene is
transcribed into three overlapping mRNAs, and we have cloned bcl-2 cDNA
sequences. Sequence analysis of the bcl-2 cDNA clones and comparison of
their sequences to their genomic counterparts indicate that the bcl-2 gene
contains at least two exons. The three bcl-2 transcripts, which
are 8.5, 5.5, and 3.5 kilobases (kb) long, overlap within the
first exon, but only the 8.5-kb and 5.5-kb transcripts contain sequences
of the second exon. The 8.5-kb and 5.5-kb transcripts seem to use
different polyadenylylation sites. Sequence analysis of the cDNA clones
corresponding to the 5.5-kb and 3.5-kb mRNAs indicates that the two bcl-2
transcripts carry two overlapping open reading frames, one of which is 717
nucleotides long and codes for a protein (bcl-2.
alpha.) of 239 amino acids and a molecular mass of 26 kDa, while
the other codes for a protein of 205 amino acids (bcl-2β, molecular
mass 22 kDa) that is identical to bcl-2.alpha
. except at the carboxyl terminus. The bcl-2 protein products in
follicular lymphomas with or without bcl-2 rearrangements are
identical to the normal bcl-2 products.

L22 ANSWER 36 OF 36 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on
STN
AN 1990:50171 BIOSIS
DN PREV199089027535; BA89:27535
TI STRESS-RESISTANCE CONFERRED BY HIGH LEVEL OF BCL-2-
ALPHA PROTEIN IN HUMAN B LYMPHOBLASTOID CELL.
AU TSUJIMOTO Y [Reprint author]
CS THE WISTAR INST ANAT BIOL, 3601 SPRUCE ST, PHILADELPHIA, PA 19104, USA
SO Oncogene, (1969) Vol. 4, No. 11, pp. 1331-1336.
CODEN: ONCNES. ISSN: 0950-9232.
DT Article
FS BA
LA ENGLISH
ED Entered STN: 11 Jan 1990
Last Updated on STN: 11 Jan 1990
AB High levels of human bcl-2 protein(s) result in (i) the tumorigenic
conversion of mouse NIH3T3 cells, (ii) the better survival of mouse

myeloid cells in the absence of the required growth factor and (iii) give
a growth advantage to human EBV-lymphoblastoid B cells both in low serum
medium and limiting dilutions. The effect of the high levels of bcl-2
protein in EBV-B cells was further investigated. This revealed that high
levels of bcl-2α protein made EBV-B
cells more resistant to a variety of stresses including the application of
heat shock, ethanol, methotrexate and the absence of serum. Stress
resistance was not observed in EBV-B cells with elevated level of c-myc
protein. The mechanism of stress resistance conferred by the bcl-2α protein is yet to be determined although the
resistance does not seem to be the result of an increase in major heat
shock proteins, hsp70 and hsp90, nor the arrest of cells in G1/G0 phase.
The increased viability was observed in control transfectants but not in
bcl-2 transfectants when cells are seeded at higher density in
the absence of serum. Thus the improved survival of cells as result of
high levels of the bcl-2α protein is
not specific to the absence of growth factor but is found to occur with a
variety of stresses.

=> s bcl 2 alpha (3a) mRNA
L23 9 BCL 2 ALPHA (3A) MRNA

=> dup rem l23
PROCESSING COMPLETED FOR L23
L24 5 DUP REM L23 (4 DUPLICATES REMOVED)

=> d bib abs 1-
YOU HAVE REQUESTED DATA FROM 5 ANSWERS - CONTINUE? Y/(N):y

L24 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2008 ACS on STN DUPLICATE 1
AN 1999:107273 CAPLUS
DN 130:148830
TI Growth hormone prevents human monocytic cells from Fas-mediated apoptosis
by up-regulating Bcl-2 expression
AU Haeffner, Astrid; Deas, Olivier; Mollereau, Bertrand; Estaquier, Jerome;
Mignon, Alexandre; Haeffner-Cavaillon, Nicole; Charpentier, Bernard;

Senik, Anna; Hirsch, Francois
CS Equipe Immunologie Cellulaire Transplantation, CNRS-UPR 420, Villejuif,
F-94801, Fr.
SO European Journal of Immunology (1999), 29(1), 334-344
CODEN: EJIMAF; ISSN: 0014-2980
PB Wiley-VCH Verlag GmbH
DT Journal
LA English
AB Apoptosis and particularly Fas-mediated apoptosis was proposed to play a key role in controlling monocyte homeostasis. The authors and others have documented the regulatory function of human growth hormone (hGH) on monocytic cells, which prompted us to investigate the role of hGH on their response to Fas antigen crosslinking. Using human promonocytic U937 cells constitutively producing hGH upon gene transfer and human primary monocytes cultured in the presence of recombinant hGH, the authors demonstrated that hGH diminished Fas-mediated cell death by enhancing the expression of the antiapoptotic oncoprotein Bcl-2 as well as the level of bcl-2α mRNA. In parallel, the authors established that overexpression of Bcl-2 through gene transfer into normal U937 cells also diminished Fas-induced apoptosis. As a result of Bcl-2 overexpression, the authors found that hGH greatly depressed Fas-induced activation of the Cys protease caspase-3 (CPP32), which in turn affected the cleavage of poly(ADP-ribose) polymerase. These data provide evidence that hGH mediates its protective effect through a Bcl-2-dependent pathway, clearly a crucial step in enhanced survival of monocytic cells exposed to Fas-induced death.
RE.CNT 59 THERE ARE 59 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2008 ACS on STN
AN 1999:360377 CAPLUS
DN 131:183383
TI Alzheimer's disease-related gene expression in the brain of senescence accelerated mouse
AU Wei, Xiaolong; Zhang, Yongxiang; Zhou, Jinhuang

CS Beijing Institute of Pharmacology and Toxicology, Beijing, Peop. Rep.
China
SO Neuroscience Letters (1999), 268(3), 139-142
CODEN: NELED5; ISSN: 0304-3940
PB Elsevier Science Ireland Ltd.
DT Journal
LA English
AB The levels of Alzheimer's disease (AD)-related genes, including β-amyloid precursor protein(APP), presenilin-1 (PS-1), PS-2, apoE, tau, c-fos, neural cell adhesion mol. 180 (NCAM-180), TGF-β1, IL-1α/β, IL-6, TNF-α/β, α-2-Macroglobulin (α2M), class II major histocompatibility antigen Ia (MHCII Ia), bcl-2α, glucocorticoid receptor-α (GRα) and mineralocorticoid receptor (MR) mRNAs were determined by reverse transcription polymerase chain reaction (RT-PCR) in the hippocampus and cerebral cortex of senescence accelerated mouse (SAM). The levels of TGF-β1, IL-1α, TNF-β, c-fos, NCAM-180, PS-1 and APP mRNAs were normally expressed in SAMP8 compared with age-matched other subline that is resistant (SAMR1). The levels of apoE, GRα and MR mRNAs in the hippocampus of SAMP8, especially GRα, were evidently lower than those in the hippocampus of SAMR1. While bcl-2α, PS-2 and tau mRNA levels of SAMP8 were significantly higher than those of SAMR1. Inflammatory cytokines (IL-1β, IL-6, TNF-α), α2M and MHCII Ia antigen mRNAs were not detected in the brain of SAM. The differences of gene expression in the cerebral cortex were less evident than in the hippocampus. The results indicated that some genes abnormally expressed in the AD brain were also found in the brain of SAMP8, which may contribute to its age-related deterioration of learning and memory. The authors' results also suggested that functional and pathol. changes which occurred in the brain of SAMP8 possessed some different aspects in comparison with the AD in consideration of the differences in gene expression.
RE.CNT 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2008 ACS on STN
AN 1996:647522 CAPLUS
DN 125:272311

OREF 125:50873a,50876a
TI Apoptosis and expression of bcl-2 α , β mRNA isoforms and protein in neuroblastoma
AU Mazzocco, K.; Scaruffi, P.; Gambini, C.; Negri, F.; Tonini, G. P.
CS Advanced Biotechnology Center, G. Gaslini Institute, Genoa, 16132, Italy
SO Apoptosis (1996), 1(1), 63-68
CODEN: APOPFN; ISSN: 1360-8185
PB Rapid Science Publishers
DT Journal
LA English
AB The authors studied apoptosis in 36 neuroblastomas by DNA ladder assay.
Expression of bcl-2α and β mRNA isoforms and protein were detected by RT-PCR and by immunohistochem., resp. Internucleosomal DNA fragmentation was found in 20/36 (56%) tumor tissues collected both at onset and relapse of disease.
Bcl-2α and β mRNAs and protein were found in almost all examined tumors irresp. of DNA ladder, thus showing lack of correlation with the clin. stage. BCL-2 protein was observed to be expressed at various levels in undifferentiated and in more differentiated neuroblasts, while the stroma and the fibrovascular tissue were neg. The results show that apoptosis is present in neuroblastoma at all stages and that bcl-2 gene is widely expressed in tumor tissue. In this series of neuroblastomas, bcl-2 expression was not correlated with unfavorable prognosis.

L24 ANSWER 4 OF 5 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
DUPLICATE 2
AN 1994:127756 BIOSIS
DN PREV199497140756
TI Developmental regulation of bcl-2 expression in the thymus.
AU Moore, N. C. [Reprint author]; Anderson, G.; Williams, G. T.; Owen, J. J. T.; Jenkinson, E. J.
CS Centre Clinical Res. Immunology Signalling, Med. Sch., Univ. Birmingham, Birmingham B15 2TT, UK
SO Immunology, (1994) Vol. 81, No. 1, pp. 115-119.
CODEN: IMMUAM. ISSN: 0019-2805.
DT Article
LA English
ED Entered STN: 24 Mar 1994

Last Updated on STN: 24 Mar 1994
AB An important factor in shaping the T-cell receptor (TcR) repertoire during thymocyte development is the susceptibility of double-positive (CD4+ CD8+) thymocytes to induction of apoptosis (negative selection) when the TcR is engaged by 'self'-antigens. Recent evidence has suggested that this susceptibility to apoptosis may be influenced by the expression of bcl-2, a proto-oncogene known to increase the resistance to apoptosis in various cell systems. Using a semi-quantitative polymerase chain reaction (PCR) technique in conjunction with staged embryonic material and purified thymocyte subpopulations we have investigated patterns of bcl-2 expression during normal T-cell development. Our results show that while bcl-2-alpha gene expression is readily detectable in immature CD3- CD4- CD8- thymocytes and in mature single-positive TcR-hi cells, it is drastically reduced in TcR negative double-positive (CD3- CD4+ CD8+) cortical thymocytes of intermediate maturity. Careful mapping of bcl-2-alpha re-expression in relation to the onset of TcR expression within the population of embryonic thymocytes indicates that bcl-2-alpha is up-regulated as soon as TcR molecules are expressed on the surface of CD4+ CD8+ thymocytes. Therefore, thymocytes susceptible to apoptosis on TcR ligation express bcl-2-alpha mRNA suggesting that changing levels of bcl-2 expression are unlikely to be the only determinant regulating susceptibility to apoptosis in the thymus. The possible implications of these changes in bcl-2 expression regarding other facets of thymocyte development will be discussed.

L24 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2008 ACS on STN DUPLICATE 3
AN 1993:252039 CAPLUS
DN 118:252039
OREF 118:43710h,43711a
TI The bcl-2 gene is highly expressed during neurogenesis in the central nervous system
AU Abe-Dohmae, Sumiko; Harada, Nobuhiro; Yamada, Kazuyo; Tanaka, Ryo
CS Med. Sch., Nagoya City Univ., Nagoya, 468, Japan

SO Biochemical and Biophysical Research Communications (1993), 191(3), 915-21
CODEN: BBRCA9; ISSN: 0006-291X
DT Journal
LA English
AB An anal. method for quantitation of the RNA transcripts of murine bcl-2
gene was developed. The PCR products from bcl-2α and bcl-2β
mRNA were fluorometrically analyzed and their specific contents were
calculated by the internal standard method. Both bcl-2 mRNAs in adult mice were
transcribed at the highest level in the thymus and at a comparable level
in the spleen. Aside from the immune system, the brain gave the most
abundant levels of the bcl-2 mRNAs. The ratios of bcl-2β
mRNA to bcl-2α mRNA
in the thymus and spleen were significantly higher than those in other
tissues. During development of the brain, the bcl-2α and
bcl-2β mRNA levels were highest on embryonic day 15, and about two
and three times higher than those of adult, resp. The results suggest
that the bcl-2 gene functions to regulate development and survival of
neurons in the central nervous system.

=> s 3 UTR and bcl 2
L25 69 3 UTR AND BCL 2

=> s l25 and PY<=1998
L26 8 L25 AND PY<=1998

=> dup rem l26
PROCESSING COMPLETED FOR L26
L27 4 DUP REM L26 (4 DUPLICATES REMOVED)

=> d bib abs 1-
YOU HAVE REQUESTED DATA FROM 4 ANSWERS - CONTINUE? Y/(N):y

L27 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2008 ACS on STN
AN 1998:672675 CAPLUS
DN 129:271496
OREF 129:55245a,55248a
TI Viral vectors for identification of RNA regulatory sequences and interacting molecules
IN Blau, Helen M.; Spicher, Albert; Guicherit, Oivin
PA The Board of Trustees of the Leland Stanford Junior University, USA

SO PCT Int. Appl., 64 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9842854	A1	19981001	WO 1998-US6093	19980327 <--

W: CA, JP
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

PRAI US 1997-42543P P 19970327

AB Methods and compns. for the identification, characterization and isolation of regulatory RNA sequences are provided. Regulatory RNA sequences mediate post-transcriptional regulation in response to various environmental conditions and can be used to alter the level of expression of endogenous genes or to identify factors which interact with regulatory RNA sequences. The invention addnl. provides improved vector systems for rapid screening, anal., and tightly-regulated expression of regulatory RNA sequences. The regulatory properties of highly conserved regions (HCRs) within 3'-UTRs that have retained greater than 70% homol. within stretches of 100 nucleotides over 30 million years were examined A retroviral vector system was used with a selectable marker that allowed rapid delivery of 3'-UTR-reporter constructs to populations of thousands of cells within one to two weeks, avoiding problems associated with clonal anal. and long-term selection. Addnl., this vector is modular, thereby permitting direct comparison of different HCRs on gene expression, independent of 5'-UTRs, promoters, protein coding regions and polyadenylation signals. Ten HCRs (from c-fos, c-myc, transferrin receptor, bcl2, EF1α, vimentin, ornithine decarboxylase, fibronectin, HuD and Ran genes) were examined Nine of these HCRs (i.e., all except the Ran HCR) were found to decrease mRNA stability to different extents. Two HCRs (the c-fos and vimentin HCRs) altered mRNA translation

under steady-state conditions. Four HCRs (the HuD, Ran, fibronectin and ornithine decarboxylase HCRs) mediated responses to changes in mitogen level by increasing reporter protein levels 2-fold while 2 HCRs exhibited a 6-fold difference in their response to another environmental stress, hypoxia.

RE.CNT 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2008 ACS on STN
AN 1997:607952 CAPLUS
DN 127:303779
OREF 127:59271a,59274a
TI Rapid molecular cloning of rearrangements of the IGHJ locus using long-distance inverse polymerase chain reaction
AU Willis, T. G.; Jadayel, D. M.; Coignet, L. J. A.; Abdul-Rauf, M.; Treleaven, J. G.; Catovsky, D.; Dyer, M. J. S.
CS Academic Department of Haematology and Cytogenetics, Haddow Laboratories, Institute of Cancer Research-Royal Marsden Hospital, Surrey, SM2 5NG, UK
SO Blood (1997), 90(6), 2456-2464
CODEN: BLOOAW; ISSN: 0006-4971
PB Saunders
DT Journal
LA English
AB Clonal rearrangements of the Ig heavy chain (IGH) locus consisting of either intrachromosomal VDJ rearrangements or interchromosomal translocations are a consistent feature of all B-cell malignancies and may be used both diagnostically and to monitor response to therapy. Many of these rearrangements are targeted to the IGHJ segments, but only some can be amplified with regular polymerase chain reaction (PCR) techniques. To permit PCR amplification of potentially all IGHJ rearrangements, we have devised a method incorporating self-ligation of restriction endonuclease-digested DNA fragments with long-distance PCR (long-distance, inverse PCR [LDI-PCR]). We show here, using only 4 nested oligonucleotide primers, the successful amplification and DNA sequencing of all IGHJ rearrangements up to 5.4 kb in length from a panel of 13 cases and cell lines of various types of B-cell malignancy. In all cases, both VDJ and

DJ IGH rearrangements and translocation breakpoints were amplified. Six cases exhibited t(14;18)(q32;q21). All translocation breakpoints were cloned and sequenced. Three cases exhibited a rearrangement to the BCL2 major breakpoint region (MBR). However, 2 other cases exhibited rearrangements between the MBR and the minor cluster region (mcr). These 2 cases broke within 44 bp of each other, confirming the presence of an addnl. 3' BCL2 breakpoint cluster region. The final case fell immediately 3' of the 3' UTR of the BCL2 gene adjacent to an Alu repeat. No other BCL2 breakpoints within this region have been reported. Four cases exhibited t(11;14)(q13;q32). All 3 cases with translocations targeted to the IGHJ segments were successfully amplified and sequenced, including 1 case in which the BCL1 translocation could not be detected by DNA blot using the currently available probes. All three translocation breakpoints fell outside the BCL1 major translocation cluster between 20 and 40 kb telomeric and showed no clustering. Two of the three fell within or adjacent to Alu repeat regions. LDI-PCR is a simple and robust technique that allows PCR amplification of nearly all IGHJ rearrangements.

RE.CNT 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 3 OF 4 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
DUPLICATE 1
AN 1997:69518 BIOSIS
DN PREV199799368721
TI Cloning of the 3' end of rat bax-alpha and corresponding developmental down-regulation in differentiating primary, cultured oligodendrocytes.
AU Madison, Dana L. [Reprint author]; Pfeiffer, Steven E.
CS Dep. Microbiol., MC-3205, University of Connecticut Sch. Med., Farmington, CT 06030, USA
SO Neuroscience Letters, (1996) Vol. 220, No. 3, pp. 183-186.
CODEN: NELED5. ISSN: 0304-3940.
DT Article
LA English

OS Genbank-U59184
ED Entered STN: 11 Feb 1997
Last Updated on STN: 25 Mar 1997
AB Bax-alpha is thought to form heterodimers with Bcl-2 and prevent apoptotic cell death. A sequence was isolated from oligodendrocyte cDNA corresponding to the uncloned 3' end of the rat bax-alpha coding region and part of the 3' UTR via a degenerate polymerase chain reaction (PCR)-based cloning method. The rat bax-alpha clone is 96 and 91% homologous to mouse and human clones, respectively, and the 3' UTR demonstrates high homology with the cloned human 3' UTR. Northern analysis demonstrated that the 1.0 kb bax-alpha mRNA species was predominant. bax-alpha mRNA is expressed in mitotic, oligodendrocyte progenitors, and is subsequently down-regulated 2-fold in differentiating oligodendrocytes.

L27 ANSWER 4 OF 4 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
DUPLICATE 2
AN 1996:414837 BIOSIS
DN PREV199699137193
TI A bcl-2/IgH antisense transcript deregulates bcl-2 gene expression in human follicular lymphoma t(14;18) cell lines.
AU Capaccioli, S.; Quattrone, A.; Schiavone, N.; Calastretti, A.; Copreni, E.; Bevilacqua, A.; Canti, G.; Gong, L.; Morelli, S.; Nicolin, A. [Reprint author]
CS Dep. Pharmacol., Sch. Med., Via Vanvitelli 32, 20129 Milan, Italy
SO Oncogene, (1996) Vol. 13, No. 1, pp. 105-115.
CODEN: ONCNES. ISSN: 0950-9232.
DT Article
LA English
ED Entered STN: 10 Sep 1996
Last Updated on STN: 10 Sep 1996
AB The 14;18 chromosome translocation, characteristic of most human follicular B-cell lymphomas, juxtaposes the bcl-2 gene with the IgH locus, creating a bcl-2/IgH hybrid gene. By mechanisms that are still under investigation, this event increases the cellular levels of the bcl-2 mRNA and thereby induces an overproduction of the antiapoptotic BCL-2 protein which is likely responsible for neoplastic transformation. In an effort to identify potential upregulators of bcl-2 activity in t(14;18) cells, we found, by strand-specific RT-PCR, a hcl-2 antisense

transcript that is present in the t(14;18) DOHH2 and SU-DHL-4 but not in the t(14;18)-negative Raji and Jurkat lymphoid cell lines, and thus appears to be dependent on the bcl-2/IgH fusion. This antisense transcript is a hybrid bcl-2/IgH RNA, that originates in the IgH locus, encompasses the t(14;18) fusion site and spans at least the complete 3' UTR region of the bcl-2 mRNA. To achieve some insight into its biological function, we treated the t(14;18) DOHH2 cell line with oligonucleotides (ODNs) by specifically targeting the bcl-2/IgH antisense strand. These ODNs lowered bcl-2 gene expression, inhibited neoplastic cell growth by inducing apoptosis. We would like to propose the hypothesis that the bcl-2 /IgH antisense transcript may contribute, by an unknown mechanism, to upregulation of bcl-2 gene expression in t(14;18) cells. The possibility has been considered that the hybrid antisense transcript mask AU-rich motifs present in the 3' UTR of the bcl-2 mRNA characterized in other genes as mRNA destabilizing elements.

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CA SUBSCRIBER PRICE	-20.00	-27.20

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